

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

PHS 2003-1

**SOLICITATION OF
THE PUBLIC HEALTH SERVICE
FOR**

**SMALL
BUSINESS
INNOVATION
RESEARCH
CONTRACT PROPOSALS**

**PROPOSAL RECEIPT DATE
NOVEMBER 8, 2002**

Internet: <http://grants.nih.gov/grants/funding/sbir.htm>

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APPENDIX E: [STATEMENT OF WORK SAMPLE FORMAT](#) - USE FOR PHASE II AND FAST TRACK PROPOSALS

APPENDIX F: [SUMMARY OF RELATED ACTIVITIES](#) - USE FOR PHASE II AND FAST TRACK PROPOSALS

APPENDIX G: [PROPOSAL SUMMARY AND DATA RECORD](#)- USE FOR PHASE II AND FAST TRACK PROPOSALS

The Appendices noted above are in Adobe Acrobat Reader fillable format.

NOTE: Other software packages for completing these applications may be available from other sources; however, it is essential that the type size and format specifications are met or the application will be returned without review.

DISCLAIMER: Reference to these software packages neither constitutes nor should be inferred to be an endorsement or recommendation of any product, service, or enterprise by the National Institutes of Health, any other agency of the United States Government, or any employee of the United States Government. No warranties are stated or implied.

U. S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

**SOLICITATION OF THE PUBLIC HEALTH SERVICE FOR
SMALL BUSINESS INNOVATION RESEARCH (SBIR)
CONTRACT PROPOSALS**

I. GENERAL PROGRAM DESCRIPTION

The Small Business Innovation Research Program recently was reauthorized by the enactment of the Small Business Reauthorization Act of 2000, (Public Law 106-554) through Fiscal Year 2008. The authorizing SBIR legislation requires two significant programmatic changes:

- Commercialization Plan. All Phase II proposals must include a succinct commercialization plan (Product Development Plan). See instructions in *Section V.3.* for specific details.
- Data Collection Requirement. Each Phase II offeror will be required to provide information for the Small Business Administration (SBA) Tech-Net Database System. See SBA's Tech-Net website (<http://tech-net.sba.gov/>) for specific details.

The Public Health Service (PHS), Department of Health and Human Services (HHS), and certain other Federal agencies must reserve 2.5 percent of their current fiscal year extramural budgets for research or research and development (R/R&D) for a Small Business Innovation Research (SBIR) program. The objectives of the SBIR Program include stimulating technological innovation in the private sector, strengthening the role of small business in meeting Federal R/R&D needs, increasing private sector commercialization of innovations developed through Federal SBIR R&D, increasing small business participation in Federal R&D, and fostering and encouraging participation by socially and economically disadvantaged small business concerns and women-owned small business concerns in the SBIR program.

The SBIR program consists of three separate phases:

Phase I: Feasibility
\$100,000
6 months

The objective of Phase I is to determine the scientific or technical feasibility and commercial

merit of the proposed research or R&D efforts and the quality of performance of the small business concern, prior to providing further Federal support in Phase II. Phase I awards normally may not exceed \$100,000 for direct costs, indirect costs, and profit (fixed fee) for a period normally not to exceed 6 months.

Phase II: Full R/R&D Effort
\$750,000
2 years

The objective of Phase II is to continue the research or R&D efforts initiated in

Phase I. Funding shall be based on the results of Phase I and the scientific and technical merit and commercial potential of the Phase II proposal. Phase II awards normally may not exceed \$750,000 for direct costs, indirect costs, and negotiated fees for a period normally not to exceed two years. That is, generally, a two-year Phase II project may not cost more than \$750,000 for that project. *Phase II proposals may only be submitted upon the request of the Contracting Officer, if not submitted concurrently with the initial Phase I proposal under the Fast-Track procedure (described in Section V.) Only one Phase II award may result from a single Phase I SBIR contract.*

Phase III: Commercialization
stage without SBIR
funds

The objective of Phase III, where appropriate, is for the small business concern to pursue

with non-Federal funds the commercialization objectives resulting from the results of the research or R&D funded in Phases I and II. In some Federal agencies, Phase III may involve follow-on, non-SBIR funded R&D or production contracts for products or processes intended for use by the U.S. Government.

Please direct questions of a general nature about the NIH SBIR Program to:

Ms. Jo Anne Goodnight
NIH SBIR/STTR Program Coordinator

6705 Rockledge Drive
Rockledge I, Room 3534
Bethesda, MD 20892
Phone: (301) 435-2688 Fax: (301) 480-0146
E-mail: sbir@od.nih.gov

or

Ms. Kay Etzler
NIH SBIR/STTR Program Analyst
6705 Rockledge Drive
Rockledge I, Room 3522
Bethesda, MD 20892
Phone: (301) 435-2713 Fax: (301) 480-0146
E-mail: sbir@od.nih.gov

A. PURPOSE OF SOLICITATION

The purpose of this Solicitation is to *invite Phase I contract proposals from small business* concerns that have the expertise to contribute to the mission of the awarding components identified below and to provide the opportunity for the submission of Phase II contract proposals concurrently with Phase I (see specific topics listed in Section XII and identified as accepting Fast-Track proposals.)

Included are instructions for offerors to prepare contract proposals, a description of the proposal review process, and some conditions of a contract award. *Contract proposals will be accepted only if they respond specifically to a research topic within this Solicitation (see Section XII "Research Topics.")* Otherwise, proposals will be returned to the offeror(s) without evaluation.

B. AWARDING COMPONENTS

The following awarding components of the PHS are participating in this SBIR Solicitation for Contract Proposals.

National Institutes of Health (NIH)

- National Institute on Alcohol Abuse and Alcoholism (NIAAA)
- National Cancer Institute (NCI)
- National Institute on Drug Abuse (NIDA)
- National Institute of Environmental Health Sciences (NIEHS)

- National Institute of General Medical Sciences (NIGMS)
- National Institute of Mental Health (NIMH)
- National Heart, Lung and Blood Institute (NHLBI)

Centers for Disease Control and Prevention (CDC)

- National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP)
- National Center for HIV, STD, and TB Prevention (NCHSTP)
- National Center for Infectious Diseases (NCID)
- National Immunization Program (NIP)

To apply for an SBIR grant rather than a contract, use the [Omnibus Solicitation of the Public Health Service for Small Business Innovation Research Grant Applications](#).

C. SBIR PROGRAM ELIGIBILITY

Organizational Criteria: Each organization submitting a proposal under the SBIR program must qualify as a small business concern (defined in Section III.) In determining whether an offeror is a small business concern, an assessment will be made of several factors, including whether or not it is independently owned and operated and whether or not it is an affiliate of a larger organization whose employees, when added to those of the offeror organization, exceed 500. In conducting this assessment, all appropriate factors will be considered, including common ownership, common management, and contractual relationships.

In accordance with 13 CFR 121.3, affiliation exists when "... one concern controls or has the power to control the other ... control may be affirmative or negative and it is immaterial whether it is exercised so long as the power to control exists." One of the circumstances that would lead to a finding that an organization is controlling or has the power to control another organization involves sharing common office space and/or employees and/or other facilities

(e.g., laboratory space). 13 CFR 121.3 also states that control or the power to control exists when “key employees of one concern organize a new concern ... and serve as its officers, directors, principal stockholders, and/or key employees; and one concern is furnishing or will furnish the other concern with subcontracts, financial or technical assistance, and/or other facilities, whether for a fee or otherwise.”

Access to special facilities or equipment in another organization is permitted (as in cases where the SBIR awardee has entered into a subcontractual agreement with another institution for a specific, limited portion of the research project). However, research space occupied by an SBIR contractor organization must be space that is available to and under the control of the SBIR contractor for the conduct of its portion of the project. Where there is indication of sharing of common employees, a determination will be made on a case-by-case basis of whether or not such sharing constitutes control or the power to control.

Whenever a proposed SBIR project is to be conducted in facilities other than those of the offeror organization, a letter must be submitted *with* the proposal stating that leasing/rental arrangements have been negotiated for appropriate research space (i.e., space that will be available to and under the control of the SBIR contractor organization).

This letter must be signed by an authorized official of the organization whose facilities are to be used for the SBIR project. It also must include a description of the facilities and, if appropriate, equipment that will be leased/rented to the offeror organization.

All SBIR contract proposals will be reviewed with the above considerations in mind. If it appears that an offeror organization does not meet eligibility requirements, the PHS will request a size determination of the organization from the cognizant Small Business Administration (SBA) regional office. The evaluation of the proposal for scientific merit will be deferred until the SBA provides a determination.

Principal Investigator Criteria. The primary employment of the principal investigator must be with the offeror at the time of contract award and during the conduct of the proposed project. PHS policy defines a principal investigator as the single individual designated in the contract proposal with responsibility for the scientific and

technical direction of the project. Primary employment means that more than one half of the principal investigator's time is spent in the employ of the small business concern. Primary employment with a small business concern precludes full-time employment at another organization.

In the event that the principal investigator: (1) is a less-than-full-time employee of the small business, (2) is concurrently employed by another organization, or (3) gives the appearance of being concurrently employed by another organization, whether for a paid or unpaid position, at the time of submission of the proposal, it is essential that documentation be submitted with the proposal to verify his/her eligibility. If the principal investigator also is employed or appears to be employed by an organization other than the offeror organization (e.g., a university, a nonprofit research institute, or another company), a letter must be provided by the non-offeror organization confirming that the principal investigator will, if awarded an SBIR contract, become a less-than-half-time employee of such organization and will remain so for the duration of the SBIR project. If the principal investigator is employed by a university, the Dean's Office must provide such a letter. If the principal investigator is employed by another for-profit organization, the corporate official must sign the letter. This documentation is required for every proposal that is submitted, even one that is a revision of a previously submitted proposal.

Performance Site Criteria. For both Phase I and Phase II, the research or R&D project activity must be performed in its entirety in the United States (see Section III. Definitions).

Market Research. The PHS will not support any market research under its SBIR program. Neither will it support studies of the literature that will lead to a new or expanded statement of work. Literature searches where the commercial product is a database are acceptable. For purposes of the SBIR program, “market research” is the systematic gathering, recording, computing, and analyzing of data about problems relating to the sale and distribution of the subject of the research project. It includes various types of research, such as the size of potential market and potential sales volume, the identification of consumers most apt to purchase the products, and the advertising media most likely to stimulate their purchases. However,

“market research” does not include activities under a research plan or protocol that require a survey of the public as part of the objective of the project to determine the impact of the subject of the research on the behavior of individuals.

II. AGENCY CONTACT FOR INFORMATION

Questions on the administration of the PHS SBIR contract program should be directed to the contracting officers listed in Section X. Contracting Officers and Addresses for Mailing and Delivery of Proposals.

The PHS SBIR Contract Solicitation ***is available in electronic PDF format*** on the NIH’s “Small Business Funding Opportunities” home page at <http://grants.nih.gov/grants/funding/sbir.htm> **Printed copies of the Solicitation will not be distributed.** The Table of Contents includes direct links and cross-references to specific sections of the document. Text searches are possible using the “binocular” icon. ***The Phase I and Phase II forms have been modified to enable the fields to be filled in directly using Adobe Acrobat Reader software, which is free.***

HELP AND INSTRUCTIONS are available for printing and viewing Acrobat files. Information on ***Fillable PDF Forms*** is also available.

NOTE: Other software packages for completing these applications may be available from other sources; however, it is essential that the type size and format specifications are met or the application will be returned without review.

DISCLAIMER: Reference to these software packages neither constitutes nor should be inferred to be an endorsement or recommendation of any product, service, or enterprise by the National Institutes of Health, any other agency of the United States Government, or any employee of the United States Government. No warranties are stated or implied.

III. DEFINITIONS

Clinical Research. NIH defines human clinical research as: **(1)** Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues,

specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are *in vitro* studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, or (d) development of new technologies. **(2)** Epidemiologic and behavioral studies. **(3)** Outcomes research and health services research. Note: Studies falling under Exemption 4 for human subjects research are not considered clinical research by this definition.

Commercialization. The process of developing markets and producing and delivering products for sale (whether by the originating party or by others); as used here, commercialization includes both government and private sector markets.

Contract. An award instrument establishing a binding legal procurement relationship between a funding agency and the recipient, obligating the latter to furnish an end product or service and binding the agency to provide payment therefore.

Essentially Equivalent Work. This term is meant to identify “scientific overlap,” which occurs when: (1) substantially the same research is proposed for funding in more than one proposal (contract proposal or grant application) submitted to the same Federal agency; OR (2) substantially the same research is submitted to two or more different Federal agencies for review and funding consideration; OR (3) a specific research objective and the research design for accomplishing that objective are the same or closely related in two or more proposals or awards, regardless of the funding source.

Funding Agreement. Any contract, grant, cooperative agreement, or other transaction entered into between and Federal agency and any small business concern for the performance of experimental, developmental, or research work funded in whole or in part by the Federal Government.

Innovation. Something new or improved, including research for: (1) development for new technologies, (2) refinement of existing technologies, or (3) development of new applications for existing technologies. For purposes of PHS programs, an example of

“innovation” would be new medical or biological products, for improved value, efficiency, or costs.

Key Personnel Engaged on Project. This term is meant to identify those individuals who contribute in a substantive way to the scientific development or execution of the project, whether or not salaries are requested.

Prototype. A model of something to be further developed that includes designs, protocols, questionnaires, software, devices, etc.

Research or Research and Development (R/R&D). Any activity that is:

1. A systematic, intensive study directed toward greater knowledge or understanding of the subject studied.
2. A systematic study directed specifically toward applying new knowledge to meet a recognized need.
3. A systematic application of knowledge toward the production of useful materials, devices, and systems or methods, including design, development, and improvement of prototypes and new processes to meet specific requirements.

Small Business Concern. A small business concern is one that, at the time of award of Phase I and Phase II, meets all of the following criteria:

1. Is independently owned and operated, is not dominant in the field of operation in which it is proposing, has its principal place of business located in the United States, and is organized for profit;
2. Is at least 51 percent owned, or in the case of a publicly owned business, at least 51 percent of its voting stock is owned by United States citizens or lawfully admitted permanent resident aliens;
3. Has, including its affiliates, a number of employees not exceeding 500, and meets the other regulatory requirements found in 13 CFR Part 121. Business concerns, other than investment companies licensed, or state development companies qualifying under the Small Business Investment Act of 1958, 15 U.S.C. 661, *et seq.*, are affiliates of one another when either directly or indirectly:

- a. One concern controls or has the power to control the other; or
- b. A third party or parties controls or has the power to control both.

Control can be exercised through common ownership, common management, and contractual relationships. The term “affiliates” is defined in greater detail in 13 CFR 121.3-2(a). The term “number of employees” is defined in 13 CFR 121.3-2(t). Business concerns include, but are not limited to, any individual (sole proprietorship), partnership, corporation, joint venture, association, or cooperative.

Joint Ventures or Limited Partnerships. Joint ventures and limited partnerships are eligible provided the entity created qualifies as a small business concern as defined in this Solicitation.

Socially and Economically Disadvantaged Individual. A member of any of the following groups:

- Black Americans
- Hispanic Americans
- Native Americans
- Asian-Pacific Americans
- Subcontinent Asian Americans
- Other groups designated from time to time by SBA to be socially disadvantaged
- Any other individual found to be socially and economically disadvantaged by SBA pursuant to Section 8(a) of the Small Business Act, 15 U.S.C. 637(a)

Socially and Economically Disadvantaged Small Business Concern. A socially and economically disadvantaged small business concern:

1. Is one that is at least 51 percent owned by:
(a) an Indian tribe or a native Hawaiian organization, or (b) one or more socially and economically disadvantaged individuals; and
2. Whose management and daily business operations are controlled by one or more socially and economically disadvantaged individuals.

Subcontract. Any agreement, other than one involving an employer-employee relationship, entered into by a Federal Government prime contractor calling for supplies or services required solely for the performance of the prime contract or another subcontract.

United States. The 50 states, the territories and possessions of the U.S., the Commonwealth of Puerto Rico, the Trust Territory of the Pacific Islands, and the District of Columbia.

Woman-Owned Small Business Concern. A small business concern that is at least 51 percent owned by a woman or women who also control and operate it. "Control" in this context means exercising the power to make policy decisions. "Operate" in this context means being actively involved in the day-to-day management.

IV. PHASE I PROPOSAL PREPARATION INSTRUCTIONS AND REQUIREMENTS

A. LIMITATIONS ON LENGTH OF PROPOSAL

SBIR Phase I proposals shall not exceed a total of 25 single-spaced pages, including the cover sheet, cost breakdown, and all enclosures or attachments. Pages should be of standard size (8 1/2" X 11"), and the font should be no smaller than 10-point. Excluded from the 25-page limitation are cover letters, letters of commitment from collaborators and consultants and letters to determine eligibility. Unless specifically solicited by a Contracting Officer, no other appendices may be submitted, and if submitted, they will not be considered in the evaluation of scientific and technical merit.

B. PROPOSAL COVER SHEET

Complete the form identified as [Appendix A](#), and use it as the first page of the proposal. No other cover sheet should be used.

- **Topic Number.** Provide the appropriate numerical designator of the research topic for which your proposal is being submitted. If your proposal is responsive to a subtopic, provide both the topic and subtopic numbers. (A numerical or alphabetical designator precedes each topic and subtopic.)
- **Project Title.** Select a title that reflects the substance of the project. Do not use the title of the topic that appears in the Solicitation.

C. ABSTRACT OF RESEARCH PLAN

Complete the form identified as [Appendix B](#), and insert it as the second page of each proposal. Abstracts of successful proposals will be published by NIH and, therefore, should not contain proprietary information. The abstract should include a brief description of the problem or opportunity, specific aims, and a description of the effort. Summarize anticipated results and potential commercial applications of the proposed research.

D. RESEARCH PLAN

Any research proposal involving the collection of information, such as surveys or interviews, of more than nine respondents will require clearance by the U.S. Office of Management and Budget. Therefore, it is not practical to propose such an activity for Phase I, which normally has only a six-month duration.

Beginning on page three of the proposal, discuss in the order indicated the following elements:

1. **Identification and Significance of the Problem or Opportunity.** Provide a clear statement of the specific technical problem or opportunity addressed.
2. **Technical Objectives.** State the specific objectives of the Phase I effort, including the technical questions it will try to answer to determine the feasibility of the proposed approach.
3. **Work Plan.** Provide a detailed plan for the R&D to be carried out, including the experimental design, procedures, and protocols to be used. Address the objectives and the questions stated in *Item*

2 above. Discuss in detail the methods to be used to achieve each objective or task.

4. **Related Research or R&D.** Describe significant research or R&D that is directly related to the proposal, including any conducted by the principal investigator/project manager or by the proposing firm. Describe how it relates to the proposed effort and any planned coordination with outside sources. The principal investigator/project manager must persuade reviewers of his or her awareness of recent significant research or R&D conducted by others in the same scientific field.
5. **Relationship with Future R&D.**
 - a. State the results expected from the proposed approach.
 - b. Discuss the significance of the Phase I effort in providing a foundation for the Phase II R/R&D effort.
6. **Potential Commercial Applications.** Describe why the proposed project appears to have potential commercial applications, and whether and by what means the proposed project appears to have potential use by the Federal Government.
7. **Key Personnel and Bibliography of Directly Related Work.** Identify key personnel, including their directly related education, experience, and bibliographic information. Where vitae are extensive, focus on summaries of the most relevant experience or publications. Provide dates and places of employment and some information about the nature of each position or professional experience. Curriculum vitae must identify the current or most recent position.
8. **Salary Rate Limitation.** Fiscal Year (FY) 2002 is the thirteenth consecutive year for which there is a legislatively mandated provision for the limitation of salary. Specifically, the Department of Health and Human Services (HHS) Appropriation Act for FY 2002, Public Law 107-116, restricts the amount of direct salary of an individual under an NIH grant or cooperative agreement (hereafter referred to as a grant) or applicable contract to Executive Level I of the Federal Executive Pay scale. Effective January 1, 2002, the Executive Level I salary level increased to \$166,700

per year. It is anticipated that this same limit will apply in FY 2003.

9. **Consultants.** Involvement of consultants in the planning and/or research stages of the project is permitted. However, such use must be described in detail and supported by appropriate letters from each individual confirming his/her role in the project.
10. **Facilities and Equipment.** Indicate where the proposed research will be conducted. One of the performance sites must be the offeror organization. Describe the facilities to be used; identify the location; and briefly indicate their capacities, pertinent capabilities, relative proximity, and extent of availability to the project. Include clinical, computer, and office facilities of the offeror and those of any other performance sites to be used in the project.

List the most important equipment items already available for this project, noting location and pertinent capabilities of each.

Any equipment and products purchased with Government funds shall be American-made, to the extent possible.

Title to Equipment. Title to equipment purchased with Government funding by the SBIR awardee in relation to project performance vests upon acquisition in the Federal Government. However, the Government may transfer such title to an SBIR awardee upon expiration of the project where the transfer would be more cost-effective than recovery of the property.

E. CURRENT AWARDS AND PENDING PROPOSALS/APPLICATIONS

As the PHS uses both contracts and grants in its SBIR program, a small business concern may not submit both a contract proposal and a grant application for essentially the same project to the same or different awarding component(s) of the PHS. The only exception would be the submission of a grant application after a contract proposal has been evaluated and is no longer being considered for award.

While it is permissible, with proposal notification, to submit identical proposals or proposals containing a significant amount of essentially equivalent work (as defined in this Solicitation) for consideration under numerous Federal program solicitations, it is unlawful to enter into contracts or grants requiring essentially equivalent effort.

If there is any question concerning this, it must be disclosed to the soliciting agency or agencies before award.

If a firm elects to submit identical proposals or proposals containing a significant amount of essentially equivalent work under other Federal program solicitations, include a statement in each such proposal indicating the information requested in items 1-10 set forth below.

In addition, provide the information requested in items 1-10 on (a) active funding through contracts, grants, and cooperative agreements from public or private sponsors; (b) contract proposals and grant and cooperative agreement applications pending review or funding; and (c) contract proposals and grant and cooperative agreement applications about to be submitted.

1. Name and address of the funding source.
2. Type of award (contract, grant, cooperative agreement) and identifying number.
3. Title of research project.
4. Name and title of principal investigator or project manager.
5. Hours per week on the project by the principal investigator or project manager.
6. Annual costs proposed or awarded.
7. Entire period of support.
8. Date of proposal/application submission or date of award.
9. Title, number, and date of solicitations under which proposals or applications were submitted or awards received.
10. The specific applicable research topic for each SBIR proposal or application submitted or award received. Specifically identify those projects that are SBIR.

F. PRIOR SBIR PHASE II AWARDS

If the small business concern has received more than 15 Phase II awards in the prior 5 fiscal

years, submit name of awarding agency, date of award, funding agreement number, amount, topic or subtopic title, follow-on agreement amount, source, and date of commitment and current commercialization status for each Phase II. This required proposal information will not be counted toward the proposal page limitations.

G. PROPOSED COST BREAKDOWN

Complete the form identified as [Appendix C \(Contract Pricing Proposal\)](#). The cost breakdown should appear as the last section of the proposal. If some items on this form do not apply to the proposed project, they need not be completed.

- Under "Government Solicitation No.," enter "PHS 2003-1."
- If supplies are proposed, provide the quantities and the price per unit.
- Under "Direct Labor," list all key personnel by name. Support personnel may be consolidated into categories or labor classes, e.g., research assistants or data processing clerks.
- If travel is proposed, provide the following details on "Exhibit A – Supporting Schedule": destination(s); duration of trip(s); number of travelers; and cost per trip, broken down by cost elements, e.g., airfare, lodging, and meals.
- If consultants are proposed, provide name(s), rate(s), and number of hours/days.
- If a subcontract is proposed, provide the same type of detailed cost breakdown as required for Appendix C. Also provide a copy of the subcontractual agreement.
- Use "Exhibit A – Supporting Schedule" to itemize and justify all major cost elements.

Normally, at least two-thirds or 67% of the entire research or analytical effort must be carried out by the offeror, i.e., subcontracts for portions of the scientific/technical effort and consultant fees normally may not exceed 33% of the total cost breakdown.

H. STREAMLINING THE CONTRACTING PROCESS

With the Federal Acquisition Streamlining Act of 1994 and the Federal Acquisition Reform Act of 1996, a number of terms and conditions that previously applied to contracts under \$100,000 are no longer applicable. Under the SBIR program, Phase I awards, which normally may not exceed \$100,000, will reflect the streamlined contract document.

The NIH has initiated special “just in time” procedures that are designed to reduce the administrative burden on offerors without compromising the information needed during the initial evaluation of proposals. Certain documents that would previously have been required for submission with the Phase II proposal will be requested at a later stage in the evaluation process. The following documentation is part of the “just in time” procedures and offerors who elect to submit proposals under the “Fast-Track” initiative below are not required to submit this documentation with their initial Phase II business proposal:

- **Travel Policy.** The offeror's written travel policy.
- **Annual Financial Report.** The offeror's most recent annual financial report.
- **Total Compensation Plan.** Salary and fringe benefits of professional employees under service contracts.
- **Data Substantiating the Costs and Prices Proposed.** That is, payroll documentation, vendor quotes, invoice prices, etc.

I. REQUIRED EDUCATION IN THE PROTECTION OF HUMAN RESEARCH PARTICIPANTS

NIH requires education on the protection of human research participants for all individuals identified as “key personnel” before funds are awarded for contract proposals involving human subjects. For information relating to this requirement, see the following notice (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html>), which was published June 5, 2000 in the *NIH Guide for Grants and Contracts*. Prior to award, the selected contractor will be required to provide a

description of education completed in the protection of human subjects for all key personnel. While NIH does not endorse programs, there are curricula available that can provide guidance or that can be modified to provide training in this area. See <http://helix.nih.gov:8001/ohsr/newcbt> for computer-based training developed for NIH that can be downloaded at no charge and modified for use. For information on facilitating education and developing curricula, see <http://www.nih.gov/sigs/bioethics>.

J. INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH

It is NIH policy that women and members of minority groups and their subpopulations must be included in all NIH-supported biomedical and behavioral research projects involving human subjects (see <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-048.html>) unless a clear and compelling rationale shows that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research.

Exclusion under other circumstances may be based on a compelling rationale and justification. Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources. Women of childbearing potential should not be routinely excluded from participation in clinical research. This policy applies to research subjects of all ages.

The inclusion of women and members of minority groups and their subpopulations must be addressed in developing a research design appropriate to the scientific objectives of the study. Describe the composition of the proposed study population in terms of gender and racial/ethnic group, and provide a rationale for selection of such subjects. Include a description of the proposed outreach programs for recruiting women and minorities as participants.

All research projects involving human subjects are subject to the policy, whether or not they are exempt from human subject protections and Institutional Review Board (IRB) review requirements. All investigators proposing research involving human subjects should read the “NIH Guidelines On the Inclusion of Women and Minorities as Subjects in Clinical Research”, which was published in the *NIH Guide for Grants*

and Contracts (October 9, 2001.) Investigators may also obtain a copy from the contracting officers found in Section X of this Solicitation.

K. INCLUSION OF CHILDREN IN RESEARCH INVOLVING HUMAN SUBJECTS

It is NIH policy that children must be included in all human subjects research, including, but not limited to, clinical trials, conducted under a contract funded by the NIH, unless there are scientific or ethical reasons not to include them.

For purposes of this policy, a “child” is defined as an individual under the age of 21 years.

Contracts involving human subjects include categories that would otherwise be exempt from the HHS regulations for the Protection of Human Research Subjects (sections 101(b) and 401(b) of 45 CFR 46), such as surveys, evaluation of educational interventions, and studies of existing data or specimens that should include children as participants. This policy applies to both domestic and foreign research contracts.

Inclusion of children as participants in research must be in compliance with all applicable subparts of 45 CFR 46 as well as other pertinent laws and regulations, whether or not such research is otherwise exempt from 45 CFR 46. Therefore, any proposals must include a description of plans for including children, unless the offeror presents clear and convincing justification for an exclusion. In the technical proposal, the offeror should create a section titled “Participation of Children.” Provide either a description of the plans to include children and a rationale for selecting or excluding a specific age range of child, or an explanation of the reason(s) for excluding children as participants in the research.

All investigators proposing research involving human subjects should read the “NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects,” which was published in the *NIH Guide for Grants and Contracts* on March 6, 1998, and is available at <http://grants.nih.gov/grants/guide/notice-files/not98-024.html>

Investigators may also obtain copies from the contracting officers found in Section X of this Solicitation.

L. REQUIREMENT FOR ADEQUATE ASSURANCE OF PROTECTION OF HUMAN SUBJECTS

The HHS regulations for the Protection of Human Subjects, 45 CFR 46 (as amended), provide a systematic means, based on established ethical principles, to safeguard the rights and welfare of individuals who participate as subjects in research activities supported or conducted by the HHS. The requirement is that an approved assurance of compliance with the regulations must be on file with the Office for Human Research Protections (OHRP), DHHS (formerly Office for Protection from Research Risks (OPRR), NIH) before an HHS award can be made.

Neither an Institutional Review Board (IRB) review nor an OHRP-approved Assurance is required at the time the proposal is submitted or at the time that the proposals are peer reviewed.

NIH policy requires that investigators submit a general description of the Data and Safety Monitoring Plan for clinical trials (biomedical and behavioral intervention studies) as part of the research proposal. In developing your Data and Safety Monitoring Plan, you should refer to the NIH Policy For Data and Safety Monitoring (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html>). See also (<http://grants.nih.gov/grants/guide/notice-files/not98-084.html>).

A general description of a monitoring plan establishes the overall framework for data and safety monitoring. It should describe the entity that will be responsible for monitoring, and how Adverse Events (AEs) will be reported to the Institutional Review Board (IRB), the NIH Office of Biotechnology Activities (OBA), and the Food and Drug Administration (FDA) in accordance with IND or IDE regulations. Although no specific page limitation applies to this section of the application, be succinct.

The frequency of monitoring will depend on potential risks, complexity, and the nature of the trial; therefore, a number of options for monitoring trials are available. These can include, but are not limited to, monitoring by a:

- Principal Investigator (required)
- Independent individual/Safety Officer

- Designated medical monitor
- Internal Committee or Board with explicit guidelines
- Data and Safety Monitoring Board (DSMB - required for multi-site trials)
- Institutional Review Board (IRB - required)

NIH specifically requires the establishment of Data and Safety Monitoring Boards (DSMBs) for **multisite** clinical trials involving interventions that entail potential risk to the participants, **and generally for Phase III clinical trials**. Although Phase I and Phase II clinical trials may also use DSMBs, smaller clinical trials may not require this oversight format, and alternative monitoring plans may be appropriate.

A detailed Data and Safety Monitoring Plan must be submitted to the applicant's IRB and subsequently to the funding IC for approval prior to the accrual of human subjects (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html>).

The review group will consider carefully whether the proposal includes necessary safeguards to protect the rights and welfare of research participants. No contract award can be made without IRB approval. Therefore, following NIH peer review and notification of an Institute's decision to proceed with negotiations and funding, the offeror should proceed with IRB review. On request of the awarding component, OHRP will contact the offeror to provide detailed instructions for filing the necessary documents to request a Single Project Assurance (SPA).

The regulations define a "human subject" as a "living individual about whom an investigator (whether professional or student) conducting research obtains: (1) data through intervention or interaction with the individual, or (2) identifiable private information." The regulations extend to the use of human organs, tissue, and body fluids from individually identifiable human subjects as well as to graphic, written, or recorded information derived from individually identifiable human subjects. The use of autopsy materials is governed by applicable state and local law and is not directly regulated by 45 CFR 46 (as amended).

In doubtful cases, prior consultation with the Office for Human Research Protections (OHRP), DHHS, (301) 496-7041, may be of assistance.

Inappropriate designations of the non-involvement of human subjects in an SBIR project may result in delays in the review of a proposal. The OHRP, on behalf of HHS, will make a final determination of whether the proposed activities are covered by the regulations or are in an exempt category, based on the information provided in the proposal.

Any SBIR contract involving human subjects that is awarded as a result of a proposal submitted in response to this Solicitation will include the following clauses:

1. The Contractor agrees that the rights and welfare of human subjects involved in research under this contract shall be protected in accordance with 45 CFR Part 46 (as amended) and with the Contractor's current Assurance of Compliance on file with the Office for Human Research Protections (OHRP), DHHS. The Contractor further agrees to provide certification at least annually that the institutional review board has reviewed and approved the procedures which involve human subjects in accordance with 45 CFR Part 46 (as amended) and the Assurance of Compliance.
2. The Contractor shall bear full responsibility for the performance of all work and services involving the use of human subjects under this contract in a proper manner and as safely as is feasible. The parties hereto agree that the Contractor retains the right to control and direct the performance of all work under this contract. Nothing in this contract shall be deemed to constitute the Contractor or any subcontractor, agent or employee of the Contractor, or any other person, organization, institution, or group of any kind whatsoever, as the agent or employee of the Government. The Contractor agrees that it has entered into this contract and will discharge its obligations, duties, and undertakings and the work pursuant thereto, whether requiring professional judgment or otherwise, as an independent Contractor without imputing liability on the part of the Government for the acts of the Contractor or its employees.

3. If at any time during performance of this contract, the Contracting Officer determines, in consultation with the OHRP, DHHS, that the Contractor is not in compliance with any of the requirements and/or standards stated in paragraphs (1) and (2) above, the Contracting Officer may immediately suspend, in whole or in part, work and further payments under this contract until the Contractor corrects such noncompliance. Notice of the suspension may be communicated by telephone and confirmed in writing.

If the Contractor fails to complete corrective action within the period of time designated in the Contracting Officer's written notice of suspension, the Contracting Officer may, in consultation with OHRP, DHHS, terminate this contract in whole or in part, and the Contractor's name may be removed from the list of those Contractors with approved Health and Human Services Human Subject Assurances.

M. NEEDLE EXCHANGE

It is anticipated that the HHS Fiscal Year 2003 Appropriations Act will continue a restriction on using contract funds to carry out any program of distributing sterile needles or syringes for the hypodermic injection of any illegal drug.

N. BAN ON HUMAN EMBRYO RESEARCH

It is anticipated that the HHS Fiscal Year 2003 Appropriations Act will continue the ban on funding of human embryo research. Currently, contract funds may not be used for: (1) the creation of a human embryo or embryos for research purposes, or (2) research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero under 45 CFR 46.208(a)(2) and Section 498(b) of the Public Health Service Act (42 U.S.C. 289g(b)). The term "human embryo or embryos" includes any organism, not protected as a human subject under 45 CFR 46 as of the date of the Act, that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or human diploid cells. Additionally, Federal funds may not be used for cloning of human beings.

O. REQUIREMENT FOR ADEQUATE ASSURANCE OF COMPLIANCE WITH THE PHS POLICY ON HUMANE CARE AND USE OF LABORATORY ANIMALS

The PHS Policy on Humane Care and Use of Laboratory Animal (Policy) establishes a number of requirements in research activities involving live, vertebrate animals. It stipulates that an offeror organization, whether domestic or foreign, bears responsibility for the humane care and use of animals in PHS-supported research activities. The PHS Policy defines "animal" as "any live, vertebrate animal used or intended for use in research, research training, experimentation or biological testing or for related purposes." An offeror organization proposing to use animals in PHS-supported activities must file a written Animal Welfare Assurance with the Office of Laboratory Animal Welfare (OLAW), NIH. When an offeror proposes research that involves animals, but the offeror does not have an Animal Welfare Assurance on file with OLAW, on request of the awarding component, OLAW will contact the offeror and provide detailed instructions for filing the necessary document.

Neither an Institutional Animal Care and Use Committee (IACUC) nor an OLAW-approved Assurance is required at the time the proposal is submitted.
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Institutions having an Assurance with OLAW are encouraged to have an IACUC review before submitting the proposal and should furnish verification of IACUC approval with the proposal. However, an Assured organization may submit the verification of IACUC review after proposal submission but before the Initial Technical Review is initiated. If verification is not received before the Initial Technical Review meeting, the awarding component will not allow the review of the proposal.

No PHS award for research involving animals will be made unless the offeror organization is operating in accord with an approved Animal Welfare Assurance and provides verification that the IACUC has reviewed and approved the proposed activity in accordance with PHS Policy. 48 CFR Part PHS 352 requires that any contract involving live, vertebrate animals, awarded as a result of a proposal submitted in response to this Solicitation include the following clauses:

1. Before undertaking performance of any contract involving research on live, vertebrate animals, the Contractor shall register with the Secretary of Agriculture of the United States in accordance with 7 U.S.C. 2316 and 9 CFR Section 2.30. The Contractor shall furnish evidence of such registration to the Contracting Officer.
2. The Contractor shall acquire animals used in research from a dealer licensed by the Secretary of Agriculture under 7 U.S.C. 2131-2157 and 9 CFR Sections 2.1-2.11, or from a source that is exempt from licensing under those sections.
3. The Contractor agrees that the care and use of any live, vertebrate animals used or intended for use in the performance of this contract will conform with the PHS Policy on Humane Care and Use of Laboratory Animals, the current Animal Welfare Assurance, the Guide for the Care and Use of Laboratory Animals prepared by the Institute of Laboratory Animal Resources, and the pertinent laws and regulations of the United States Department of Agriculture (see 7 U.S.C. 2131 *et seq.* and 9 CFR Subchapter A, Parts 1-3). In case of conflict between standards, the more stringent standard shall be used.
4. If at any time during performance of this contract, the Contracting Officer determines, in consultation with the Office of Laboratory Animal Welfare (OLAW), National Institutes of Health (NIH), that the Contractor is not in compliance with any of the requirements and/or standards stated in paragraphs (1) through (3) above, the Contracting Officer may immediately suspend, in whole or in part, work and further payments under this contract until the Contractor corrects the noncompliance. Notice of the suspension may be communicated by telephone and confirmed in writing. If the Contractor fails to complete corrective action within the period of time designated in the Contracting Officer's written notice of suspension, the Contracting Officer may, in consultation with OLAW, NIH, terminate this contract in whole or in part, and the Contractor's name may be removed from the list of those Contractors with approved Public Health Service Animal Welfare Assurances.

The Contractor may request registration of its facility and a current listing of licensed dealers from the Animal Care Sector Office of the Animal and Plant Health Inspection Service (APHIS), USDA, for the sector in which its research facility is located. The location of the appropriate APHIS Regional Office, as well as information concerning this program, may be obtained by contacting:

Animal Care Staff
USDA/APHIS
4700 River Road, Unit 84
Riverdale, MD 20737
(301) 734-4980

Offerors proposing research that involves live, vertebrate animals will be contacted by OLAW and given detailed instructions on filing a written Animal Welfare Assurance with the PHS.

Offerors are encouraged to visit the OLAW website at <http://grants.nih.gov/grants/olaw/olaw.htm> for additional information. OLAW may be contacted at the National Institutes of Health at (301) 594-2289.

P. RESEARCH USING HUMAN EMBRYONIC STEM CELLS

<http://www.nih.gov/news/stemcell/index.htm>

In signing the proposal Cover Sheet, the duly authorized representative of the applicant organization certifies that if research using human embryonic stem cells is proposed, the applicant organization will be in compliance with the "Notice of Extended Receipt Date and Supplemental Information Guidance for Applications Requesting Funding that Proposes Research with Human Embryonic Stem Cells" (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-006.html>).

V. "FAST-TRACK" INITIATIVE

(Applicable Only to Proposals Submitted to NIH)

The "Fast-Track" initiative is a parallel review option available to those small business concerns (offeror organizations) whose proposals satisfy additional criteria that enhance the probability of the project's commercial success. This initiative is applicable only to NIH and only if an awarding component indicates it is accepting Fast Track proposals for a particular

topic. (Refer to Section XII, "Research Topics," for notation.)

The Fast-Track initiative is an opportunity for small business concerns to submit both a Phase I and Phase II proposal for concurrent peer review. This initiative also has the potential to minimize any funding gap between Phase I and Phase II.

Fast-Track Proposal Process

To identify the proposals as Fast-Track, check the box marked "Yes" next to the words "Fast-Track Proposal" shown on the Phase I Proposal Cover Sheet ([Appendix A](#)).

The small business concern must submit both a Phase I and a Phase II proposal for concurrent initial peer review and evaluation. The Fast-Track proposal must consist of the following parts:

1. **Phase I Proposal.** Prepared in accordance with Section IV. Phase I Proposal Preparation Instructions and Requirements, and addressing all factors stated in the evaluation criteria (Section VII) for Phase I proposals.
2. **Phase II Proposal.** Prepared in accordance with Section VI, Fast-Track Phase II Proposal Preparation Instructions and Requirements and addressing all factors stated in the evaluation criteria (Section VII) for Phase II proposals.
3. **Product Development Plan.** A concise document (limited to ten pages), which addresses each of the following areas:
 - a. Company information, including size, specialization area(s), products with significant sales, and history of previous Federal and non-Federal funding, regulatory experience, and record of commercializing SBIR or other research;
 - b. Value of SBIR project, including lay description of key technology objectives, current competition, and advantages to competing products or services, and any funding commitments from private sector or non-SBIR funding sources;
 - c. Commercialization plans, milestones, target dates, market analyses of market

size, and estimated market share after first year sales and after five years. The plan should state the amount and approximate dates that Phase III funds will be made available; and

- d. Patent status or other protection of project intellectual property.

Letters of Commitment. Offerors are encouraged to seek letters of interest or commitment(s) of funds and/or resources from an investor or partner organization for commercialization of the product(s) or service(s) resulting from the SBIR contract.

Fast-Track proposals that do not containing all parts described above will be redirected for Phase I consideration only.

The Phase I and Phase II proposals will be scored individually, and the scores for both phases will be totaled. Following the initial peer review, Fast-Track proposals may receive secondary review by the program staff of the respective NIH awarding component.

Fast-Track Phase II proposals may be funded following submission of the Phase I final report, and a determination that the Phase I objectives were met, feasibility was demonstrated, and funds are available.

VI. FAST-TRACK PHASE II PROPOSAL PREPARATION INSTRUCTIONS AND REQUIREMENTS

A. LIMITATIONS ON LENGTH OF PROPOSAL

SBIR Phase II proposals generally should not exceed a total of 150 single-spaced pages, including all enclosures and attachments. Pages should be of standard size (8 1/2" x 11") and the font should be no smaller than 10 point. Excluded from the page limitation are cover letters and letters from collaborators and consultants.

B. TECHNICAL PROPOSAL FORMAT AND CONTENT REQUIREMENTS

1. **Phase II Technical Proposal Cover Sheet-** Use [Appendix D](#).

2. **Table of Contents**
3. **Abstract of the Research Plan-** Use [Appendix B](#). State the broad, long-term objectives and specific aims. Do not include any proprietary information. Briefly and concisely describe the research design and methods for achieving these goals.
4. **Anticipated Results of Phase I Effort -** briefly discuss and summarize the objectives of your Phase I effort, the research activities to be carried out, and the anticipated results.
5. **Research Plan**
 - a. Detailed Approach and Methodology- provide an explicit detail description of the Phase II approach. This section should be the major portion of the proposal and must clearly show advancement in the project appropriate for Phase II. Indicate not only what is planned, but also how and where the work will be carried out. List all tasks in a logical sequence to precisely describe what is expected of the contractor in performance of the work. Tasks should contain detail to (1) establish parameters for the project; (2) keep the effort focused on meeting the objectives; (3) describe end products and deliverables; and (4) describe periodic/final reports required to monitor work progress under the contract.
 - b. Personnel- list by name, title, department and organization, the extent of commitment to this Phase II effort, and detail each person's qualifications and role in the project. **Provide curricula vitae for all key staff members**, describing directly related education, experience, and relevant publications. Describe in detail any involvement of subcontractors or consultants, and **provide curriculae vitae for all key subcontractor staff. Also, include letters of commitment with proposed consultants confirming the extent of involvement and hourly/daily rate.**
 - c. Resources- list/describe all equipment, facilities and other resources available for this project, including the offeror's clinical, computer and office facilities/equipment at any other

performance site that will be involved in this project. Briefly state their capacities, relative proximity and extent of availability to this effort. **(Any equipment specifically proposed as a cost to the contract must be justified in this section as well as detailed in the budget. Equipment and products purchased with Government funds shall be American-made, to the extent possible. Title to the equipment will vest in the Government.)**

- d. Other considerations - provide a brief narrative of any unique arrangements, safety procedures in place, animal welfare issues, human subjects, etc. Note: If the research plan includes the use of human subjects or animals, refer to paragraphs IV. I-P of this solicitation for further guidance.
- e. Appendices
 - (1) **Work Statement** - develop a Statement of Work similar in format to the sample in [Appendix E](#). Create this from your detailed approach and methodology. It will be incorporated into the final contract document.
 - (2) **Product Development Plan** – Required for ALL Phase II and Fast-Track applications. Comply with requirements referred to in *Section V.3.*)
6. **Summary of Related Activities** -use [Appendix F](#).
7. **Technical Proposal Cost Information** - use [Appendix C](#). Delete the fringe benefit costs, indirect costs and fee. Prepare a separate Appendix C for each year of the contract and a summary of the entire project.
8. **Number of Copies** -submit an original and 9 copies.

C. BUSINESS PROPOSAL FORMAT AND CONTENT REQUIREMENTS

1. **Cover Page** - use NIH Form 2043, Proposal Summary and Data Record, [Appendix G](#).

2. **Breakdown of Proposal Estimated Costs, Fee and Labor Hours** - use [Appendix C](#). Explain the basis for all costs and submit documentation to support all proposed costs must be submitted. Prepare a separate Appendix C for each year of the contract and a summary of the entire project.
3. **Number of Copies** - submit an original and 4 copies.

VII. METHOD OF SELECTION AND EVALUATION CRITERIA

Proposals will be initially screened to determine their compliance with the administrative requirements of this Solicitation and their applicability to the research topic selected by the offeror. Using the technical evaluation factors described below in Section VII.B., a peer review panel will evaluate proposals passing the initial screening for technical merit and scientific acceptability, to determine the most promising approaches.

A. EVALUATION PROCESS

Contract proposals are subjected to peer review by panels of scientists selected for their competence in relevant scientific and technical fields. The peer review panel will be responsible for evaluating proposals for scientific and technical merit and for performing a concept review, if one was not accomplished previously. The peer review panel provides a rating, makes specific recommendations related to the scope, direction and/or conduct of the proposed research, and for those proposals recommended for award, may provide a commentary about the funding level, labor mix and duration of the proposed contract project. The Institute program staff of the awarding component will conduct a second level of review. Recommendations of the peer review panel and program staff are based on judgments about not only the technical merit of the proposed research but also its relevance and potential contributions to the mission and programs of the awarding component. A Phase I or Phase II contract may be awarded only if the corresponding proposal has been recommended as technically acceptable by the peer review panel. ***Funding for any/all acceptable proposals is not guaranteed.***

B. TECHNICAL EVALUATION CRITERIA

In considering the technical merit of each proposal, the following factors will be assessed:

FACTORS FOR PHASE I PROPOSALS	WEIGHT
1. The soundness and technical merit of the proposed approach and identification of clear measurable goals (milestones) to be achieved during Phase I. <i>(Preliminary data are not required for Phase I proposals.)</i>	40%
2. The qualifications of the proposed principal investigator, supporting staff, and consultants.	20%
3. The potential of the proposed research for technological innovation.	15%
4. The potential of the proposed research for commercial application.	15%
5. The adequacy and suitability of the facilities and research environment.	10%

FACTORS FOR PHASE II PROPOSALS	WEIGHT
1. The scientific/technical merit of the proposed research, including adequacy of the approach and methodology, and identification of clear, measurable goals to be achieved during Phase II.	30%
2. The potential of the proposed research for commercialization and the adequacy of the Product Development Plan.	30%
3. The qualifications of the proposed principal investigator, supporting staff and consultants.	25%
4. The adequacy and suitability of the facilities and research environment.	15%

C. PROPOSAL DEBRIEFING

Offerors will be notified when they are no longer being considered for award. Offerors are entitled to one debriefing, which can be requested within three days of the receipt of the notification.

D. AWARD DECISIONS

For proposals recommended for award, the awarding component considers the following:

1. Ratings resulting from the scientific/technical evaluation process;
2. Areas of high program relevance;
3. Program balance (i.e., balance among areas of research); and
4. Availability of funds.

The agency is not under any obligation to fund any proposal or make any specific number of contract awards in a given research topic area. The agency may also elect to fund several or none of the proposals received within a given topic area. The SBIR contract projects do not require establishing a competitive range or requesting final proposal revisions before reaching source selection decisions.

VIII. CONSIDERATIONS

A. AWARDS

1. The award instrument will be a contract.
2. A profit or fixed fee may be included in the proposal and the fee will be negotiated. A profit or fee is considered any amount in excess of actual direct and indirect cost incurred in the conduct of a project.
3. Phase I awards will be firm fixed price contracts. Normally, Phase II awards will be cost-plus-fixed-fee contracts.
4. The average dollar value of Phase I contracts to be awarded will be approximately \$100,000. Phase II contracts normally may not exceed \$750,000—including direct costs, indirect costs, and negotiated fixed fee.

Approximate number of Phase I contract awards:

AWARDING COMPONENTS		No. OF AWARDS
National Institutes of Health	National Institute on Alcohol Abuse and Alcoholism (NIAAA)	1

AWARDING COMPONENTS		No. OF AWARDS
(NIH)	National Cancer Institute (NCI)	35
	National Institute on Drug Abuse (NIDA)	12
	National Institute of Environmental Health Sciences (NIEHS)	5
	National Institute of Mental Health (NIMH)	12 - 15
	National Institute of General Medical Sciences (NIGMS)	1
	National Heart, Lung, and Blood Institute (NHLBI)	6
Centers for Disease Control and Prevention (CDC)	National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP)	11
	National Center for HIV, STD, and TB Prevention (NCHSTP)	8
	National Center for Infectious Diseases (NCID)	2
	National Immunization Program (NIP)	2

B. FINAL REPORT

Original
plus 2 copies

A final report is required of all Phase I and Phase II contractors. It should include a detailed description of the project objectives, the activities that were carried out, and the results obtained. An original and two copies of this report must be submitted as directed by the Contracting Officer not later than the expiration date of the Phase I contract.

Each Phase II "Fast-Track" contractor must submit semi-annual progress reports. A final report is required no later than the expiration date of the Phase II contract. All reports (original plus two copies) must be submitted to the Contracting Officer.

C. PAYMENT

The Government may make payments, including invoice and contract financing payments, by electronic funds transfer (EFT). As a condition to any payment, the contractor is required to provide information required to make payment by EFT.

Payments on Phase I contracts may be made on a monthly advance basis. Invoices/financing requests submitted for costs incurred under Phase II cost reimbursement contracts will be on a monthly basis unless otherwise authorized by the contracting officer.

D. LIMITED RIGHTS INFORMATION AND DATA

Proprietary Information. Information contained in unsuccessful proposals will remain the property of the offeror. The Government, however, may retain copies of all proposals. Public release of information in any proposal will be subject to existing statutory and regulatory requirements.

The Department of Health and Human Services (HHS) recognizes that, in responding to this Solicitation, offerors may submit information that they do not want used or disclosed for any purpose other than for evaluation. Such data might include trade secrets, technical data, and business data (such as commercial information, financial information, and cost and pricing data). The use or disclosure of such information may be restricted if offerors identify it and the Freedom of Information Act (FOIA) does not require its release. For information to be protected, offerors must identify in the Notice of Proprietary Information (on the Proposal Cover Sheet) the page(s) on which such information appears. Any other Notice may be unacceptable to the Government and may constitute grounds for removing the proposal from further consideration without assuming any liability for inadvertent disclosure.

Unless disclosure is required by the FOIA, as determined by FOI officials of the HHS, data contained in those portions of a proposal that have been identified as containing restricted information, in accordance with the Notice of Proprietary Information, shall not be used or disclosed except for evaluation purposes.

The HHS may not be able to withhold data that has been requested pursuant to the FOIA, and the HHS FOI officials must make that determination. The Government is not liable for disclosure if the HHS has determined that disclosure is required by the FOIA.

If a contract is awarded to the offeror as a result of, or in connection with, the submission of a proposal, the Government shall have the right to use or disclose the data to the extent provided by law. Proposals not resulting in a contract remain subject to the FOIA.

Rights to Data Developed Under SBIR Funding Agreement. Rights to data, including software developed under the terms of any funding agreement resulting from a contract proposal submitted in response to this Solicitation, shall remain with the awardee. However, the Government shall have the limited right to use such data for internal Government purposes and shall not release such data outside the Government without permission of the awardee for a period of four years from completion of each phase of the project under which the data was generated.

Copyrights. The awardee may normally copyright and publish (consistent with appropriate national security considerations, if any) material developed with PHS support. The awarding component receives a royalty-free license for the Federal Government and requires that each publication contain an acknowledgement of agency support and disclaimer statement, as appropriate. An acknowledgement shall be to the effect that: "This publication was made possible by contract number _____ from (*PHS awarding component*)" or "The project described was supported by contract number _____ from (*PHS awarding component*)."

Patents. Small business concerns normally retain the principal worldwide patent rights to any invention developed with Government support. Under existing regulations, 37 CFR 401, the Government receives a royalty-free license for Federal Government use, reserves the right to require the patent-holder to license others in certain circumstances, and requires that anyone exclusively licensed to sell the invention in the United States must normally manufacture it substantially in the United States.

To the extent authorized by 35 U.S.C. 205, the Government will not make public any information disclosing a Government-supported invention for a four-year period to allow the awardee a reasonable time to file a patent application, nor will the Government release any information that is part of that application.

Information about additional requirements imposed by 37 CFR 401 should be obtained from local counsel or from:

Office of Policy for Extramural
Research Administration,
Extramural Inventions and Technology
Resources Branch,
National Institutes of Health (NIH)
6701 Rockledge Drive
One Rockledge Building, Room 1136, MSC 7980,
Bethesda, MD 20892-7980
phone: (301) 435-1986 fax: (301) 480-0272
e-mail: gs60a@nih.gov

Inventions must be reported promptly—within two months of the inventor's initial report to the contractor organization—to the Division of Extramural Inventions and Technology Resources, NIH, at the address above. This should be done prior to any publication or presentation of the invention at an open meeting, since failure to report at the appropriate time is a violation of 35 USC 202, and may result in loss of the rights of the small business concern, inventor, and Federal Government in the invention. All foreign patent rights are immediately lost upon publication or other public disclosure unless a United States patent application is already on file. In addition, statutes preclude obtaining valid United States patent protection after one year from the date of a publication that discloses the invention.

The reporting of inventions can be accomplished by submitting paper documentation, including fax, or electronically through the NIH Edison Invention Reporting System. Use of the Edison system satisfies all mandated invention reporting requirements and access to the system is through a secure interactive Web site <http://www.iedison.gov> to ensure that all information submitted is protected. In addition to fulfilling reporting requirements, Edison notifies the user of future time sensitive deadlines with enough lead-time to avoid the possibility of loss of patent rights due to administrative oversight. Edison can accommodate the invention reporting need of all organizations. For

additional information about this invention reporting and tracking system, visit the Edison home page cited above or contact Edison via e-mail at Edison@od.nih.gov.

Sharing Biomedical Research Resources. It is the policy of the NIH that unique research resources developed with NIH funding must be shared with the research community. Restricted availability of these resources can impede the advancement of research. Principles and Guidelines for Recipients of NIH Research Grants and Contracts, as published in the Federal Register Notice on December 23, 1999 [http://ott.od.nih.gov/NewPages/RTguide_final.html], provide assistance to determine reasonable terms and conditions for acquiring and disseminating research tools, consistent with the objectives of furthering biomedical research and adhering to the Bayh-Dole Act.

Royalties. If royalties exceed \$1,500, you must provide the following information on a separate page for each separate royalty or license fee:

1. Name and address of licensor.
2. Date of license agreement.
3. Patent numbers.
4. Patent application serial numbers, or other basis on which the royalty is payable.
5. Brief description (including any part or model number of each contract item or component on which the royalty is payable.)
6. Percentage or dollar rate of royalty per unit.
7. Unit price of contract item.
8. Number of units.
9. Total dollar amount of royalties.
10. If specifically requested by the Contracting Officer, a copy of the current license agreement and identification of applicable claims of specific patents (see FAR 27.204 and 31.205-37.)

E. PERFORMANCE OF RESEARCH AND ANALYTICAL WORK

In Phase I projects, normally a minimum of two-thirds or 67% of the research or analytical effort must be performed by the small business concern.

In Phase II projects, normally a minimum of one-half or 50% of the research or analytical effort must be performed by the small business concern.

The Contracting Officer must approve deviations from these requirements in writing.

Contractor Commitments. Upon entering into a contract, the contractor agrees, in accordance with the terms and conditions of the contract, to accept certain legal commitments embodied in the clauses of Phase I and Phase II contracts. The following list illustrates the types of clauses to which a contractor is bound. This list is not exhaustive. Copies of complete terms and conditions are available upon request.

Clauses That Apply to Contracts NOT Exceeding \$100,000

1. **Standards of Work.** Work performed under the contract must conform to high professional standards.
2. **Inspection.** Work performed under the contract is subject to Government inspection and evaluation at all times.
3. **Termination for Convenience.** The Government may terminate the contract at any time for convenience if it deems termination to be in its best interest, in which case the contractor will be compensated for work performed and for reasonable termination costs.
4. **Disputes.** Any dispute concerning the contract that cannot be resolved by agreement shall be decided by the contracting officer with right of appeal.
5. **Equal Opportunity.** The contractor will not discriminate against any employee or applicant for employment because of race, color, religion, sex, or national origin.
6. **Affirmative Action for Veterans.** The contractor will not discriminate against any employee or applicant for employment because he or she is a disabled veteran or veteran of the Vietnam era.
7. **Affirmative Action for Handicapped.** The contractor will not discriminate against any employee or applicant for employment because he or she is physically or mentally handicapped.
8. **Gratuities.** The Government may terminate the contract if any gratuities have been offered to any representative of the Government to secure the contract.
9. **American-made Equipment and Products.** When purchasing equipment or products under an SBIR contract award, the contractor shall purchase only American-made items whenever possible.

Clauses That Apply to Contracts Exceeding \$100,000

In addition to the foregoing clauses, the following clauses apply to contracts expected to exceed \$100,000.

10. **Examination of Records.** The Comptroller General (or a duly authorized representative) shall have the right to examine any directly pertinent records of the contractor involving transactions related to this contract.
11. **Default.** The Government may terminate the contract for default if the contractor fails to perform the work described in the contract and such failure is not the result of excusable delays.
12. **Contract Work Hours.** The contractor may not require an employee to work more than eight hours a day or forty hours a week unless the employee is compensated accordingly (i.e., overtime pay).
13. **Covenant Against Contingent Fees.** No person or agency has been employed to solicit or secure the contract upon an understanding for compensation except bona fide employees or commercial agencies maintained by the contractor for the purpose of securing business.
14. **Patent Infringement.** The contractor shall report each notice or claim of patent infringement based on the performance of the contract.

F. ADDITIONAL INFORMATION

1. This Solicitation is intended for informational purposes and reflects current planning. If there is any inconsistency between the information contained herein and the terms of any resulting SBIR contract, the terms of the contract are controlling.

2. Prior to award of an SBIR contract, the Government may request the offeror to submit certain organizational, management, personnel and financial information to assure responsibility of the offeror to receive an award.
3. The Government is not responsible for any expenditures of the offeror in advance and in anticipation of an award. In a cost reimbursement contract, reimbursement of costs by the Government may be made only on the basis of costs incurred by the contractor after award and during performance.
4. This Solicitation is not an offer by the Government and does not obligate the Government to make any specific number of awards. Awards under this program are contingent upon the scientific/technical merit of proposals and the availability of funds.
5. The SBIR program is not intended as a mechanism to invite unsolicited proposals. Unsolicited proposals shall not be accepted under the SBIR program in either Phase I or Phase II.
6. If an award is made pursuant to a proposal submitted in response to this SBIR Solicitation, the contractor will be required to certify that he or she has not previously been, nor is currently being, paid for essentially equivalent work by any agency of the Federal Government.
7. Prior to award of a contract, the contractor will be required to provide a Data Universal Numbering System (DUNS) number. A DUNS number may be obtained immediately, at no charge, by calling Dun and Bradstreet on (800) 333-0505.

IX. INSTRUCTIONS FOR PROPOSAL SUBMISSION

A. RECEIPT DATE

The deadline for receipt of all contract proposals submitted in response to this Solicitation is:

**5:00 p.m., Eastern Standard Time
Friday, November 8, 2002**

Any proposal received at the offices designated below after the exact time specified for receipt will not be considered unless it is received before award is made and:

1. It was sent by registered or certified mail not later than the fifth calendar day prior to the date specified for receipt of proposals;
2. It was sent by mail or hand-delivered and it is determined by the Government that the late receipt was due primarily to mishandling by the Government after receipt at the Government installation;
3. It was transmitted through an electronic commerce method authorized by the Solicitation and was received at the initial point of entry to the Government infrastructure not later than 5:00 p.m. one working day prior to the date specified for receipt of proposals;
4. It is the only proposal received, or;
5. It is received in the office designated for receipt of proposals on the first workday on which normal Government processes are resumed following an emergency or anticipated event that interrupts normal Government processes so that proposals cannot be received by the exact time specified in the Solicitation.

Despite the specified receipt date above, a proposal received after that date may be considered if it offers significant costs or technical advantages to the Government and it was received before proposals were distributed for evaluation, or within 5 calendar days after the exact time specified for receipt, whichever is earlier.

B. NUMBER OF COPIES

For Phase I, submit the original and 5 copies of each proposal. The principal investigator and a corporate official authorized to bind the offeror must sign the original. The 5 copies of the proposal may be photocopies of the original.

For Phase II, see instructions under paragraph VI.

C. BINDING AND PACKAGING OF PROPOSAL

Send all copies of a proposal in the same package. Do not use special bindings or covers. Staple the pages in the upper left corner of each proposal.

X. CONTRACTING OFFICERS AND ADDRESSES FOR MAILING OR DELIVERY OF PROPOSALS

Any small business concern that intends to submit an SBIR contract proposal under this Solicitation should provide the appropriate contracting officer(s) with early, written notice of its intent, giving its name, address, telephone, and topic number(s). If a topic is modified or canceled before this Solicitation closes, only those companies that have expressed such intent will be notified.

A. NATIONAL INSTITUTES OF HEALTH (NIH)

National Institute on Alcohol Abuse and Alcoholism (NIAAA)

Ms. Roberta Wilhelm
Phone: (301) 443-1191
Fax: (301) 443-3891
E-mail: rwilhelm@niaaa.nih.gov

Proposals to the NIAAA must be mailed or delivered to:

Ms. Roberta Wilhelm
Contracting Officer
Contracts Management Branch
National Institute on Alcohol Abuse and Alcoholism
6000 Executive Blvd., Suite 504
Bethesda, MD 20892-7003 *

**Change the city to Rockville and the zip code to 20852 if hand-delivered or delivered by an overnight service to the NIAAA.*

National Cancer Institute (NCI)

Mr. Joseph Bowe
Phone: (301) 435-3810
Fax: (301) 480-0309
E-mail: jb166i@nih.gov

Proposals to the NCI, *if mailed through the U.S. Postal Service*, must be addressed as follows:

Mr. Joseph Bowe
Contracting Officer
Research Contracts Branch,
National Cancer Institute
6120 Executive Blvd., EPS Room 6038
Bethesda, MD 20892-7222 *

**Change the city to Rockville and the zip code to 20852 if hand-delivered or delivered by an overnight service to the NCI.*

National Institute on Drug Abuse (NIDA)

Ms. Nikki Zangwill
Phone: (301) 443-6677
Fax: (301) 443-7595
E-mail: nz2f@nih.gov

Proposals to the NIDA must be mailed or delivered to:

Ms. Nikki Zangwill
Contracting Officer, Contracts Management Branch
National Institute on Drug Abuse
6001 Executive Boulevard
Room 3105, MSC 9543
Bethesda, Maryland 20892-9543 *

**Change the city to Rockville and the zip code to 20852 if hand-delivered or delivered by an overnight service to the NIDA.*

National Institute of Environmental Health Sciences (NIEHS)

Mr. Phillip D. Jones
Phone: (919) 541-0426
Fax: (919) 541-2712
E-mail: pj13c@nih.gov

Proposals to the NIEHS must be mailed or delivered to:

Mr. Phillip D. Jones
Contracting Officer
Contracts and Research Branch, DERT
National Institute of Environmental Health Sciences
P. O. Box 12874
Research Triangle Park, NC 27709

Proposals to the NIEHS, *if hand-delivered or delivered by an overnight service*, must be addressed as follows:

Mr. Phillip D. Jones
Contracting Officer
Contracts and Research Branch, DERT
National Institute of Environmental Health
Sciences
79 T.W. Alexander Drive, Building 4401
Research Commons
Research Triangle Park, NC 27709

**National Institute of General Medical
Sciences (NIGMS)**

Ms. Silver C. Jones
Contracting Officer
National Institutes of Health
Division of Research Acquisition, OLAO
6100 Executive Blvd., Room 6E01
Bethesda, Maryland 20892
Phone: (301) 496-4487
Fax: (301) 402-0178
E-mail: sj12z@nih.gov

Proposals to the NIGMS must be mailed or
delivered to:

Ms. Silver C. Jones
Contracting Officer
National Institutes of Health
Division of Research Acquisition, OLAO
6100 Executive Blvd., Room 6E01
Bethesda, Maryland 20892*

**Change the city to Rockville and the zip code to
20817 if hand-delivered or delivered by an
overnight service to the NIGMS.*

National Institute of Mental Health (NIMH)

Mr. David Eskenazi
Phone: (301) 443-2696
Fax: (301) 443-0501
E-mail: de5d@nih.gov

Proposals mailed to the NIMH must be
addressed to:

Mr. David Eskenazi
Contracting Officer
Chief, Contracts Management Branch
National Institute of Mental Health
6001 Executive Boulevard
Room 6107, MSC 9603
Bethesda, Maryland 20892-9603 *

**Change the city to Rockville and the zip code to
20852 if hand-delivered or delivered by an
overnight service to the NIMH.*

**National Heart, Lung and Blood Institute
(NHLBI)**

Mr. Robert Best
Phone: (301) 435-0330
Fax: (301) 480-3338
E-mail: best@nhlbi.nih.gov

Proposals to the NHLBI, if mailed through the
U.S. Postal Service, must be addressed as
follows:

Review Branch
Division of Extramural Affairs
National Heart, Lung, and Blood Institute
6701 Rockledge Drive
Room 7091
Bethesda, MD 20892-7924*

*Change the zip code to 20817 if hand-delivered
or delivered by an express or other courier
service to the NHLBI.

**B. CENTERS FOR DISEASE CONTROL AND
PREVENTION**

**National Center for Chronic Disease
Prevention and Health Promotion
(NCCDPHP)**

**National Center for HIV, STD, and TB
Prevention (NCHSTP)**

**National Center for Infectious Diseases
(NCID)**

National Immunization Program (NIP)

Mr. Curt Bryant
Phone: (770) 488-2806
Fax: (770) 488-2828
Email: ckb9@cdc.gov

Proposals to the NCCDPHP, NCHSTP, NCID
and the NIP must be mailed or delivered to:

Mr. Curt Bryant
CDC Small Business Program Manager
Procurement and Grants Office
2920 Brandywine Road
Atlanta, GA 30341

XI. SCIENTIFIC AND TECHNICAL INFORMATION SOURCES

Health science research literature is available at academic and health science libraries throughout the United States. Information retrieval services are available at these libraries and Regional Medical Libraries through a network supported by the National Library of Medicine. A list of Regional Medical Libraries and information about network services may be requested from the Public Information Office, National Library of Medicine, Bethesda, MD 20894, (301) 496-6308.

Other sources that provide technology search and/or document services include the organizations listed below. They should be contacted directly for service and cost information.

National Technical Information Service

5285 Port Royal Road
Springfield, VA 22161
(703) 487-4600

Mid-Atlantic Technology Applications Center

University of Pittsburgh
823 William Pitt Union
Pittsburgh, PA 15260
(412) 648-7000
(412) 648-7003 (Fax)
(800) 257-2725 (toll-free US)

Mid-Continent Technology Transfer Center

The Texas A&M University System
College Station, TX 77843-3401
(409) 845-8762
(409) 845-3559 (Fax)

Great Lakes Industrial Technology Center

25000 Great Northern Corporate Center
Suite 260
Cleveland, OH 44070-5310
(216) 734-0094

Center for Technology Commercialization

Massachusetts Technology Park
100 North Drive
Westborough, MA 01581
(508) 870-0042

Southern Technology Applications Center

University of Florida
College of Engineering
Box 24
One Progress Boulevard
Alachua, FL 32615
(904) 462-3913
(800) 225-0308 (outside FL)

Far West Regional Technology Transfer Center

University of Southern California
3716 South Hope Street, Suite 200
Los Angeles, CA 90007-4344
(213) 743-6132
(213) 746-9043 (Fax)
(800) 642-2872 (CA only)
(800) 872-7477 (outside CA)

National Technology Transfer Center

Wheeling Jesuit College
316 Washington Avenue
Wheeling, WV 26003-6295
(800) 678-6882 (toll-free US)

(All services at no cost)

XII. RESEARCH TOPICS

NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM (NIAAA)

The NIAAA supports research on the causes, prevention, control, and treatment of the major health problems of alcohol abuse, alcoholism, and alcohol-related problems. Through its extramural research programs, the NIAAA funds a wide range of basic and applied research to develop new and/or improved technologies and approaches for increasing the effectiveness of diagnosis, treatment, and prevention. The NIAAA also is concerned with strengthening research dissemination, scientific communications, public education, and data collection activities in the areas of its research programs.

This solicitation invites proposals in the following area:

024 Use of Information from the Mouse Transcriptosome and Proteome to Develop a Correlational Alcohol-Relevant Database

The mouse has become the foundation of genetic and other preclinical studies in alcoholism and related research areas (Goldman, D., Crabbe J. Prog. Neuropsychopharm. Biol. Psych. 10: 177-189, 1986). Alcoholism researchers have well exploited mouse models for genetic analysis of alcohol-related behaviors and to understand alcohol's actions in brain (Tabakoff B., Hoffman, P.L. Alcohol Res. Hlth 24: 77-84, 2000). Recent technology allows for large-scale examinations of the mouse transcriptosome and proteome (Doerge, R.W. Nature Rev Genetics 3: 43-52, 2002; Chakravarti, D.N. et al. BioTechniques Suppl. 1: 4-15, 2002). A recent NIAAA Workshop on Proteomics focused attention on how these technological advances can further the research on the etiology of alcoholism and alcohol-induced tissue damage, and how they can be used to identify medications targets for alcoholism.

To justify large-scale investment in support of proteomic research projects, several important issues can be addressed initially through a contractual mechanism to establish "proof of concept" and the utility of integration of proteomic information with gene array and genomic data in studies of alcoholism and alcohol-related organ damage.

Little or no data have appeared in the literature correlating transcriptional data to protein levels and measures of post-translational modifications in mammalian species. Knowing the relationship between transcriptional data and protein levels, particularly in experiments with ethanol, is of significant importance since ethanol can perturb cellular systems at various levels to generate damage or neuroadaptation leading to tolerance and dependence on ethanol. Data also need to be collected for calibrating the performance of custom arrays and commercial products such as the Affymetrix "chip" arrays. Proprietary information issues, periodic changes in commercial chip properties and commercial company closures make long-term experiments using commercial devices inappropriately risky for purposes of comparison and development of sound databases.

The purpose of this announcement is to generate a contractual agreement with a group possessing a demonstrated capacity to perform, analyze, store and distribute transcriptional and translational data utilizing animal and cellular models of high relevance to alcohol research. Transcriptional data should be obtained on both "custom" arrays and Affymetrix arrays containing a minimum of 12,000 mouse gene probes. Protein translational information should be obtained with the most current techniques that can examine a vast array of cellular proteins simultaneously. Informatics expertise and equipment needs to be available to the contractor to make definitive comparisons between the different gene array methodologies, and between the transcriptional and proteomic information. The contractor should have the means in place to allow access to this database by the alcohol research community.

The following are examples of experimental systems and techniques (not exclusive of others) that should be considered for use by the contractor:

- Utilize *selected lines of mice* which, for instance, differ in their development of acute functional tolerance to alcohol. Assay relevant tissues at different exposure time points.
- Utilize transgenic mice in which an alcohol-sensitive signaling molecule (protein kinase or adenyllyl cyclase) has been overexpressed or "knocked out" in brains of animals on at least two genetic backgrounds.
- Use cerebellar granule neurons grown in culture in the presence and absence of ethanol.
- Examine gene expression in whole brain and targeted brain areas (e.g., hippocampus, amygdala, striatum, prefrontal cortex and cerebellum) using commercial and custom arrays which simultaneously examine expression of >12,000 mouse genes.
- Examine neuroadaptive changes in gene expression in cerebellar granule cells produced by exposure of these cells to different doses of ethanol (0-50 mM) for at least four days.

- Examine changes in the proteome in the animal brains and in cells in culture (same as above) using state of the art proteomic techniques, including laser desorption, “*in situ*” trypsinization of proteins on two-dimensional gels, creation of protein blots for archiving experiments, and mass spectroscopic analysis of proteins for identity and quantity.
- Use state-of-the-art informatics and statistical techniques for comparing transcriptional and translational events and profiles, focusing on identity of gene products and description of functional characteristics of known gene products (mRNA and protein).
- Discover alcohol-induced changes and inherent predisposing elements (mRNA and protein) to alcohol's effects that are not yet catalogued and characterized in genomic and proteomic databases.

PHASE I: Set up custom microarray as well as commercial array (e.g., Affymetrix, etc) with initial comparison of expression profiles and at different concentrations of ethanol exposure. Set up proteomic analysis the same tissues under the same ethanol concentrations as in the genomic analysis. At the end of Phase I, it is anticipated that at least one set of analyses will be performed, analyzed and stored in the database.

PHASE II: In the second year, results of the initial survey will be expanded to analyzing at least 12,000 genes and a full complement of corresponding proteins. A database, or databases, containing this transcriptional and proteomic data affected genes and proteins will be established and made.

NATIONAL CANCER INSTITUTE (NCI)

The NCI is the Federal Government's principal agency established to conduct and support cancer research, training, health information dissemination, and other related programs. As the effector of the National Cancer Program, the NCI supports a comprehensive approach to the problems of cancer through intensive investigation in the cause, diagnosis, prevention, early detection, treatment, rehabilitation from cancer, and the continuing care of cancer patients and families of cancer patients. To

speed the translation of research results into widespread applications, the National Cancer Act of 1971 authorized a cancer control program to demonstrate and communicate to both the medical community and the general public the latest advances in cancer prevention and management.

This Solicitation invites proposals in the following areas:

181 Clinical Trial Data Collection Using Hand-Held Technology

(Fast-Track proposals will be accepted)

The National Cancer Institute is soliciting systems to support streamlined clinical trial data collection, using handheld technology. This solicitation addresses two specific areas of interest. *Offerors are invited to address any or all areas.* The areas are: support of imaging data collection and cancer treatment trial data collection and reporting.

Imaging Data Collection:

NCI, in support of its cancer clinical trials imaging network, the American College of Radiology Imaging Network (ACRIN), is interested in further improving the collection of relevant data in these trials. ACRIN has developed a totally digital web-based system for its activities. However, case report forms are still used at the point of participant contact and are a source of error and inefficiency.

The successful offeror shall research and develop a solution (system) to capture in an electronic form at the point of participant contact subject and clinical trial data. The system developed shall also enable full integration of said data into a database such as the existing web-based ACRIN system. In addition the offeror will use the available CDE (Common Data Elements), CTC (Common Toxicity Criteria), CTSU (Clinical Trials Support Unit) data requirements and standards and other electronic requirements and standards being developed specifically for imaging clinical trials. New informatics solutions to allow advanced terminology searching, creation of protocol specific lists of adverse events for screening, and point-of care coding of data for later transfer to central databases are sought. The new tools should provide research investigators and data collection personnel with tools to improve

completeness and accuracy of data entry, and reduce redundant data entry into multiple systems. The system shall with minimal effort, replicate any case report form used in ACRIN trials. NCI in collaboration with ACRIN will identify and coordinate users to be included in beta testing, and the knowledge acquisition (KA) phases of this effort. NCI will provide ongoing guidance and monitor compliance with the stated standards.

Treatment Trials Data Collection:

The Cancer Treatment Evaluation Program, CTEP, has been advancing recommendations for the streamlining of cancer clinical trials. Several of the pilot projects have demonstrated areas where efficiencies can be achieved. One such area is the data collection of clinical trials data. Over the past several years, CTEP has developed several data standards and streamlined approaches, including Common Data Elements for trials, the Common Toxicity Criteria, and the Cancer Trials Support Unit. Industry and others have adopted much of this work. CTEP proposes this SBIR topic to exploit these products and projects.

The current paradigm is to use paper reports, mail them to operations offices, or carry the paper to networked computers, and enter the data. When errors are found, the paper case report form is taken back to medical records areas, corrected, and the data is then once again entered. CTEP is requesting SBIR proposals for the development of integrated and automated applications to improve efficiency and timeliness this current paradigm. Advances in hardware and software standards have allowed the routine integration of informatics tools in numerous business and clinical data collection environments.

The successful offeror shall fully utilize the CDE (Common Data Elements), CTC (Common Toxicity Criteria), and CTSU data requirements and standards. In particular, a significant expansion of the CTC in both volume of elements and complexity is under current development with the goal of including full surgical and late effects. New informatics solutions will be needed to allow advanced terminology searching, creation of protocol specific lists of adverse events recommended for screening, and point-of care coding of data for later transfer to central databases. The new tools should provide research investigators and

data collection personnel with tools to improve completeness and accuracy of data entry, reduce redundant data entry into multiple systems, and perhaps add features not currently available in a non-electronic paradigm. The system developed shall also integrate with the commercial Oracle Clinical product, the repository system for the CTSU. The system developed shall, with minimal effort, replicate any case report form, using the information stored in the CTSU, CDE, and CTC repositories.

CTEP will identify and coordinate users to be included in beta testing, and the knowledge acquisition, KA, phase of this effort. CTEP will provide ongoing guidance and monitor compliance with the stated standards.

It is anticipated that Phase 1 of this task will be to design a feasible approach of integrating the resulting system with CTSU's Oracle Clinical Database. Phase II will be development and deployment of the system.

182 Development of Oligonucleotide Selection Software for Molecular Genetic Analysis

(Fast-Track proposals will be accepted)

The National Cancer Institute is seeking proposals to develop oligonucleotide (primer/probe) selection software for integration into Bioinformatics Laboratory Information Management Systems. Publicly available software (e.g., on <http://www.hgmp.mrc.ac.uk/GenomeWeb/nuc-primer.html>) exists to design oligonucleotide primers for the polymerase chain reaction (PCR), the basis of molecular genetic analysis of DNA (sequencing and genotyping). Many companies have developed proprietary software for primer selection, either included in program packages like Vector Nti (www.informax.com), as stand-alone programs (<http://www.lifescience-software.com/products/body/oligo/oliinfo.htm>), or on the web-sites of companies synthesizing oligonucleotide primers (e.g., <http://www.epochbio.com/Ordering/index.htm>). However, there are no packages that design oligonucleotide primers/probes for a variety of molecular genetic analysis platforms, where the hybridization requirements for oligonucleotide primers and probes can be complex and specific to individual platforms. This solicitation is aimed at the development of a software program

package that could be used to design oligonucleotide primers and probes for multiple genotyping platforms with the necessary specificity. This type of software will be a crucial component in the implementation of high throughput genotyping at the NCI and in the extramural scientific community. In addition, the integration of this type of software into the laboratory information management systems (LIMS) that are currently available will be crucial to the bioinformatics efforts associated with high throughput genotyping. This solicitation requires the contractor to:

1. Develop a series of programs that perform oligonucleotide primer and/or probe selection using theoretical and experimental biophysical parameters for:
 - a) PCR, PCR-RFLP, PCR, PCR and cycle-sequencing;
 - b) primer-extension genotyping:
 - i) for single-plex and multiplex for genotype determination using MALDITOF (mass spec) (e.g., Buetow et al., Proc Natl Acad Sci U S A. 98:581-4, 2001) and capillary analysis methods (e.g., Syvanen, Hum Mutat. 13(1):1-10, 1999);
 - ii) for single-plex allele frequency estimation in DNA pools using MALDITOF (e.g., Ross et al., Biotechniques, 29(3):620-6, 628-9, 2000) and capillary analysis (e.g., Matyas, Hum Mutat 19:58-68, 2002);
 - c) allele-specific PCR for allele frequency estimation in pools (e.g., Germer & Higuchi, Genome Research, 10:258-266, 2000) or genotyping in individual samples (e.g., Bottema and Sommer, Mutation Res 288:93-102, 1993);
 - d) PCR primers and allele-specific hybridization probes for genotyping using methods such as TaqMan™ (e.g., Livak, Genet Anal, 14:143-149, 1999), FP (Kwok, Human Mutation, Hum Mutat 19:315-23, 2002 and DASH (Prince et al., Genome Res 11:152-62, 2001).

Phase I - the goal will be to demonstrate the development of a program package that will perform the design in a stand alone program. The program should be demonstrated to work in

a nationally recognized genotyping facility in a university or governmental institutional setting which regularly utilizes most of the molecular genetic analysis techniques described above (e.g., all but d or all but c), i.e., in a core facility serving a research institute or department. The offeror shall identify and work with the facility's IT, bioinformatics and wet-laboratory staff to implement and test the program package to validate the design capabilities of the program package. The program package must run on standard computer workstations and be multi-user accessible over standard intranets. A validation experiment designed by the facility's staff that utilizes the molecular genetic analysis techniques must be performed and incorporated into a final report by which the capability of the program package can be judged.

2. Integrate the software programs into:
 - a) the bioinformatics modules of the currently available LIMS, i.e., relational databases storing sequence text files linked to genes and genetic polymorphisms. This requires a graphical user interface to select and interact with a particular program, and a method to import a list of sequences for primer/probe design without operator interaction after selection of a particular program
 - b) an e-commerce engine permitting the investigator to purchase designed oligonucleotides from a vendor using a credit card or institutional purchase arrangement.

Phase II - the offeror will develop, implement and integrate the program package into (1) an existing bioinformatics module that supports the bioinformatics activity of a nationally recognized genotyping facility in a university or governmental institutional setting as in the Phase I requirement, and (2) integrate the e-commerce engine into the facility's institutional accounting system. The offeror shall identify and work with the bioinformatics, administrative and accounting personnel at the chosen institution to implement the design programs of the program package into the bioinformatics platform in use at the facility and the e-commerce engine of the program package into the accounting system in use at the institution. Demonstrated use of the program package by both the bioinformatics staff and the use of the e-commerce engine by

the institution must be the criterion for successful completion of the research project. Fast-track proposals are encouraged in response to this solicitation.

183 Particle-Based Flow Cytometric Assay for Detection and Quantification of Viral Antibodies

(Fast-Track proposals will be accepted)

The NCI is seeking proposals to develop assays for the detection and quantification of serum or plasma antibodies directed against several viral antigens. Historical and recent data suggest that detection and quantification of antibodies against certain viral antigens are predictive of subsequent risk of cancer or other serious diseases. However, progress in this area has been limited by serologic techniques developed in the last century, many of which require subjective interpretation, and by the substantial labor and other costs required for titering to quantify antibody reactivities. With the recent development of particle-based flow cytometric assays, it may be possible to overcome many of these limitations. The general principle is that a conventional immunoassay is performed on a flow cytometer, using microspheres as the solid support. The recently developed particle-based flow cytometric systems are particularly promising, as they enable the simultaneous detection and quantification of up to 100 proteins in microliter quantities of serum or plasma. This topic focuses on the detection and quantification of human antibodies directed against known antigens. Of special interest are the antigens of hepatitis C virus (HCV) and Kaposi's sarcoma herpesvirus [KSHV, also known as human herpesvirus 8 (HHV-8)], Epstein-Barr virus (EBV) and human T-lymphotropic virus type I (HTLV-I). An effective assay is expected to have immediate application to a broad range of research in viral epidemiology at the NCI and the broader extramural scientific community, as well as potential application to the clinical assessment and care of patients. An effective assay is likely to serve as a prototype applicable to detection and quantification of many other foreign and human antigens.

Under Phase I, the goal for the offerors will be to demonstrate proof-of-concept that a particle-based flow cytometric assay can be used to detect human antibodies. Of special interest are four HCV antigen (NS5, c100, c33c, and c22) and three specific KSHV antigens (K8.1,

orf73/LNA1, and orf65). Offerors may want to include additional HCV antigens, KSHV antigens, EBV antigens, or HTLV-I antigens. The offeror will procure the recombinant proteins or synthetic peptides from commercial or non-commercial sources. If needed, NCI can provide the KSHV recombinant proteins and 0.5mL of six human sera or plasma specimens with known reactivity against the HCV and KSHV antigens. An offeror that includes EBV or HTLV-I antigens can be provided sera or plasma specimens with known antibody reactivity to those agents. The contractor shall provide all other reagents and equipment to resolve the chemistry, antigen stability on the coated beads, labeling characteristics, detection signals, reproducibility, computer analysis of the data, and other issues required to optimize simultaneous detection of the serum or plasma antibodies without mutual interference. The final deliverable for Phase I shall be a comprehensive and detailed report by which proof-of-concept can be judged.

In Phase II, the offeror shall develop an assay kit that detects and quantifies all antibodies simultaneously. Deliverables shall be a kit consisting of a complete set of reagents, computer analysis software compatible with commercially available software packages, and instructions sufficient for detection and quantification of the antibodies. Fast-track proposals are encouraged in response to this solicitation.

184 Biomedical Informatics System for Basic and Clinical Cancer Research

Basic science discoveries in molecular biology, genomics, and genetics are increasingly relevant to the improved classification, diagnosis, and treatment of human cancer. The NCI is committed to promoting the development and deployment of enabling technologies that take advantage of the surge of bioinformatic data and transform it into knowledge that is directly applied to patient diagnosis and therapy decisions. The NCI is seeking proposals from vendors who are investigating the design and construction of software or data management systems that integrate genomics data with patient, drug, and clinical information. Proposals should describe how these systems will support high throughput gene sequence and expression technologies, ontologies, drug and agent information, clinical research data, and controlled vocabularies. Proposals should also

describe how the system would implement appropriate security to insure compliance with federal mandates for patient data privacy. NCI and other public data interchange and infrastructure standards should be addressed.

Deliverables for Phase I Awards:

- Written requirements for a system for cancer research that incorporates molecular genetic, genomic, agent, and clinical data.
- Design document for the system. This document should identify NCI and other genomic and clinical data sources to be used for implementation and describe the strategy for their integration. Public standards for clinical and basic science data should be addressed. The approach to insuring patient clinical and genetic data security while still enabling advanced research and data mining applications must be included. Tools, algorithms, and statistical methods that operate on gene sequence, expression, pathology, and clinical measurement data to be used in the system should be described.
- Universal Modeling Language (UML) models of all architectural components.
- Prototype software and database system demonstrating proof of principle of a selection of components.

Deliverables for Phase II Awards:

- Implementation strategy and project plan for a full working system.
- A full working software and database system that implements the market-validated features, functions and requirements developed in Phase I.
- Technical documentation of the system, including UML models, system architecture, programming interfaces, and supporting software requirements.

185 Development of Novel Agents Directed Against Childhood Cancer Molecular Targets

(Fast-Track proposals will be accepted)

The Cancer Therapy Evaluation Program (CTEP) supports the development of anti-cancer agents specifically designed to modulate molecular targets. Although chromosomal abnormalities, fusion proteins, altered and chimeric transcriptional control genes, and other molecular alterations have been identified for many adult and pediatric tumors (see chart below), childhood cancer is not a focus of commercial pharmaceutical drug discovery. Furthermore, pediatric investigators have developed xenograft, transgenic and syngeneic *in vivo* tumor models, as well as *in vitro* models, for many childhood cancers that can be utilized in the development of novel treatment approaches. In order to exploit new advances in molecular drug development for pediatric cancer, CTEP proposes this SBIR topic to support the early identification, biological characterization, and preclinical testing of agents specifically aimed at childhood cancer molecular targets.

Proposals submitted in response to this solicitation should be focused on the discovery and development of a specific agent or class of agents. Proposals may include development of lead agents already identified or very early initiatives to identify and characterize agents from a library of potential compounds. "Early" initiatives should describe the screening methods to be employed and the library of agents to be screened so that their potential pediatric cancer relevance can be appreciated. All proposals should describe the molecular rationale for the potential agent's interaction with the target molecule(s) and the logical mechanism of malignant-cell death induced by the proposed agent(s). There should also be a rationale as to why the agent(s) are applicable to pediatric malignancies. A detailed plan for early preclinical testing of the agent(s) to establish its potential relevance for pediatric cancer treatment must be provided. The successful offeror will likely have previous expertise in creating small molecule or other targeted agents, as well as preclinical testing. The method of agent synthesis or generation should be described as fully as possible.

It is recognized that within the constructs of the SBIR program there may not be full funding for preclinical drug development of some agents. Thus, offerors will be encouraged to identify a co-funding partner or other sources of support. If so, the proposal should specify the company, partner, or other funds and/or resources to be

dedicated to activities directly related to the SBIR project and describe those activities.

Following is a list of identified molecular entities associated with pediatric malignancies. Submissions can be targeted at any of these molecular entities or to other relevant targets.

PEDIATRIC MALIGNANCY	
Rhabdomyosarcoma	PAX3-FKHR PAX7-FKHR
Ewings sarcoma	EWS-FLI1 EWS-ETV1 EWS-ERG
Desmoplastoic round cell sarcoma	EWS-WT1
Wilms tumor	WT1, WT2
Neuroblastoma	TRK A, B or C MYCN
Hepatoblastoma	Abnormal β -catenin
Lymphoblastic leukemia	TEL-AML1 MLL Gene Rearrangements TAL1 Gene Rearrangements
Myeloid leukemia	ETO-AML1 MLL Gene Rearrangements
Lymphoma	NPM-ALK C-Myc

Proposal selection will be based upon:

1. target relevance to pediatric malignancy
2. proposed means of target interaction and cancer cell death induction
3. apparent feasibility of agent production

4. innovator's demonstrated ability to develop and produce similar targeted agents
5. feasibility of agent preclinical testing

Phase I proposals should seek to establish the technical, scientific merit, and feasibility of identifying novel agents that modulate in a potentially therapeutic manner a molecular target relevant to one or more childhood cancers. For example, at the end of phase I, the offeror may have identified through use of a screening method available to the offeror a series of compounds that appear to specifically modulate the target of interest. Phase II proposals should extend phase I findings to identify a candidate agent that modulates the molecular target of interest and that is potentially suitable for clinical evaluation.

186 Target Based High Throughput Screening for the Identification of Radioprotectors

(Fast-Track proposals will be accepted)

The successful application of radiotherapy as a cancer treatment modality is severely constrained by the risk for normal tissue injury. Because approximately half of all cancer patients receive radiation treatment, the ability to selectively protect normal tissue would be of obvious clinical benefit. In addition to cancer therapy, current geopolitical circumstances reinforce the need for generating agents that protect against the consequences of environmental radiation exposure, accidental or intentional. Currently, there are relatively few available agents with the potential to reduce or eliminate radiation-induced normal tissue injury after clinical and/or environmental exposure. A goal of the Radiation Research Program is to support the identification and development of novel radioprotectors. Towards this end, we are inviting proposals that apply target based high throughput screening strategies to the discovery of radioprotective agents.

A major obstacle to the development of radioprotectors has been a deficiency in the understanding of the processes (cellular and molecular) responsible for radiation-induced normal tissue injury. However, recent studies have begun to identify critical events in the pathogenesis of radiation injury that occur in a number of tissues and, importantly, that may be

susceptible to manipulation. High throughput screening has been a frequent first step used in industry and academia for the identification of compounds that target specific molecules or cellular processes. The successful offeror will develop and perform high throughput approaches for the identification of agents that affect molecules or processes that play critical roles in the expression of radiation induced normal tissue injury. The offeror should have access to chemical and/or combinatorial libraries and targets can include, but are not limited to, radiation-induced apoptosis and TGF β -mediated gene expression. The NCI will provide ongoing guidance and monitor progress.

It is expected that lead compounds against a defined target involved in normal tissue radioresponse will be identified through the application of HTS. The compounds should then be validated in cell-based *in vitro* systems. A list of the validated compounds will serve as the deliverables.

187 Expert- vs. User-Tailored Interactive Media

(Fast-Track proposals will be accepted)

The majority of World Wide Web programs for health promotion, disease prevention and disease management require users to tailor their own educational experiences and most of these Web-based programs and print-based tailored programs have employed expert systems to generate feedback to users. Determining which population groups should use *expert-tailored* or *user-tailored* interactive multimedia interventions could help proliferate the use of interactive communication technologies for cancer prevention and control-related behaviors. Distinctions between the two formats have been found to be important in computer-assisted instruction research. Some research indicates that the use of an *expert-tailored* system will result in higher rates of health behavior change than the *user-tailored* system. However, these distinctions have not been sufficiently tested.

In Phase I, this solicitation requires the offeror to test the feasibility of developing a system to determine when an *expert-tailored* system or a *user-tailored* system should be used and with what populations. In Phase II, the offeror is required to (a) develop, test, and compare a *user-tailored* interactive media format, that relies on the subject to control the health education

experience by self-selecting topics and their sequence with an *expert-tailored* interactive multimedia format that relies on a diagnostic, algorithmic system to tailor the cessation education experience; (b) address user, topic and expert factors of both systems; (c) evaluate how the use of information influences behavioral change; (d) determine which system is most appropriate for different types of populations, (e) determine in what situations and environments it is best to use a user-tailored format versus an expert-tailored format.

188 Technologies to Promote Best Practices in Data Sharing

(Fast-Track proposals will be accepted)

While the National Institutes of Health (NIH) recognizes the need to protect patentable and other proprietary data and the restriction on data sharing that may be imposed by agreements with third parties, data sharing promotes many goals of the NIH and the National Cancer Institute's research endeavor. Data sharing provides a source of unique data that cannot be readily replicated; allows scientists to expedite the translation of research results into knowledge, products, and procedures to improve human health; reinforces open scientific inquiry; encourages diversity of analysis and opinion; promotes new research; makes possible the testing of new or alternative hypotheses and methods of analysis; supports studies on data collection methods and measurement; facilitates the education of new researchers; enables the exploration of topics not envisioned by the initial investigators; and permits the creation of new data sets when data from multiple sources are combined. More importantly, data sharing minimizes the collection of similar information by more than one applicant and would allow funding of more applicants.

In Phase I, this solicitation requires the offeror to test the feasibility of developing a system for data sharing and develop alternatives for perceived barriers. In Phase II, the offeror is required to adhere to the guidelines for data sharing in

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-035.html> and (a) identify the entire spectrum of ways for sharing research data and test the impact of each method to determine best practices for reaching the broadest possible scientific community in the

most cost-effective manner; (b) identify the best methods for data sharing for different kinds of research studies including those that have sensitive data such as those dealing with human subjects; (c) develop and test new and innovative methods for data sharing; (d) evaluate the outcomes of data sharing policies including measure such as expedition of the translation of research results into knowledge, products, and procedures to improve the public health; and (e) develop points of dissemination.

189 Real-Time Cancer Communications Data Collection

(Fast-Track proposals will be accepted)

Global self-report and diaries are commonly used to collect data about behaviors and experiences of cancer patients and at risk populations; studies of the impact of risk communication collect self-report data on the impact of communication on day-to-day experience and behavior change; clinical trials of cancer treatments use diaries to collect data on pain and side effects. Yet, studies of the cognitive process suggest that reporting of such data based on recall is error-prone and biased. An improved methodological approach uses Ecological Momentary Assessment (EMA) to assess behavior, thoughts, and feelings in real time and in the natural environment. Written diaries have been commonly used to reduce reliance on recall and get real-time data to implement EMA strategies. However, paper-based diary methods often produce poor quality data and are often completed in batches and in retrospect, undermine the key objective of the diary method. A recent study demonstrated that *most* of the paper diary entries by patients (79%) were falsified, casting doubts on the validity of the data collected through paper-based methods of self-report. Recent developments in informatics tools and methods now apply handheld and web technology to the collection of diary data, allowing very high rates of documented compliance to be achieved. The methodology includes methods for collecting meta-data about the respondent's compliance and using such data to measure and improve compliance. These technological and methodological developments have also enabled implementation of improved assessment designs, such as intensive random sampling of respondent behavior. Most of these tool tools, however, are proprietary, thus limiting their availability to widespread adoption in

academic cancer communications, cancer control, and clinical oncology research.

In a Phase I, this solicitation requires the offeror to study the feasibility of developing a user-configurable application service provider software application capable of deploying real-time diary solutions for use in cancer control research. In a Phase II, the offeror is required to (a) convene a group of experts to discuss the new informatics data gathering tools and best procedures, content and format for cancer control research applications; (b) develop and validate informatics tools for collecting real-time data from respondents in their natural environment, and tools to enable researchers to design and implement EMA approaches to cancer control research; (c) develop tools for collecting, summarizing, and reporting process data to meet emerging standards for scientific reporting of EMA studies; (d) evaluate use of the new informatics data-gathering tools with relevant audiences in key settings and determine impact on quality of data collected; and (e) determine the best methods for using the informatics data-gathering tools with different audiences and different research topics.

190 New Approaches for the Determination of 3-Dimensional Protein Structure

(Fast-Track proposals will be accepted)

Structure determination has proved to be an integral component of modern cancer biology and therapy research. The atomic understanding gives new insights into protein function and potential drug inhibitors. While the number of structures determined continues to rise, the number of potential targets and protein-protein interactions needing understanding outpaces it. The recent explosion in genomic and expression profiling data exacerbates this situation. Currently, the majority of protein structure studies utilizes high-powered x-ray sources or nuclear magnetic resonance (NMR). Both of these approaches, while invaluable, are inherently costly and time consuming. The development of new technologies and approaches would not only accelerate discovery but also may generate new insights into structural biology. The purpose of this solicitation would be to develop novel and practical technologies for the determination of higher-level protein structure. The new approach should be compatible with current protein purification schemes and standards. Novel

methodologies to facilitate and automate the preparation of samples for structure analysis will also be appropriate. Structural data generated should be portable and useful in the generation of 3-Dimensional protein models.

Phase I proposals should be used to demonstrate the technical and scientific merit and feasibility of the proposed project. Under the phase II proposal the methods and/or equipment should be finalized and its commercial potential demonstrated.

191 Technologies for the Study of Genetic Alterations

(Fast-Track proposals will be accepted)

Central to the theme that cancer is a genetic disease is the identification and understanding of the genetic events and mutations responsible. These events can occur early during the initiation phase or later during progression, including metastasis. To facilitate a better understanding of these genetic and epigenetic events, the NCI encourages the development of molecular detection mechanisms. In support of this, three of the current NCI Extraordinary Opportunities are directly related to this topic. Despite the advances made in the last 5 years in cancer genomics, the sheer size and complexity of the human genome is a continued source of technical challenges. Application of the current advances in genomic information requires specific refinement and tool development. Specific examples of potential tools include application of BAC (bacterial artificial chromosomes) clones for specific identification of human cancer genes, development of oligo-nucleotide libraries for SNP (single nucleotide polymorphism) analysis, development of reagents and oligo-nucleotide primers libraries for genomic screens. Whole genomic maps of cancer aberrations based on existing and de-novo data would also be appropriate. This solicitation seeks specific tools and reagents to facilitate the identification of cancer genes and their understanding. These tools or reagents should also be portable and developed as a reliable resource for the community.

The purpose of the Phase I would be to explore the practicality and novelty of the proposed technical approach. In the phase II, the contractor would be responsible for the full implementation and commercial development of tools or reagents that facilitate the identification

of human cancer genes, incorporating the current array of genomic data.

192 New Technologies for Monitoring the Tumor Micro-environment

(Fast-Track proposals will be accepted)

While cancer is characterized as a specific malignant cell type, it has become clear that, as a disease, cancer involves the environment in which it grows. It follows then, that to adequately understand cancer, one must also understand the influences and interactions of the cancer cell's microenvironment. The tumor microenvironment has been recognized as a future Extraordinary Opportunity for the NCI. The tumor micro-environment has come to encompass various components and/or structures of cells and tissues. One of the most important components associated with the micro-environment is the vascularization or angiogenesis critically associated with tumor development and metastasis. Other areas of interest include cell-cell signaling, physical interactions and barriers, characterization of specific cell types, induction of epithelial cell and mesenchymal cell lineages, tumor-immune cell interaction, vascular mimicry, and the very signals that produce tumor stroma. While many of the individual components or proteins have been identified, there is a need to understand the "communication" and interactions that exist within this environment. These involve physical, chemical, and electrical interactions among the various cells and molecules. There also exist a need for specific physical and computational models to assist in the understanding and prediction of cell-stroma interactions. New insights in the disease environment will facilitate our understanding and treatment of the disease. In order to better understand these critical components of the disease of cancer, we will need new tools and approaches unique for these types of interaction.

The proposals should identify a specific aspect of the cellular microenvironment and develop an appropriate monitoring technology. In the phase I, this technological approach's ability and feasibility should be demonstrated. This could include but would not be limited to: protein identification and concentration, intercellular signaling, membrane biology, biochemical and electrical monitoring, and physical interactions. Proposed approaches should be sensitive to the special conditions and aspects of the cellular

microenvironment. Both *in vitro* and *in vivo* approaches will be appropriate. The phase II would witness further development and testing of these technologies in a biologically relevant setting with the eventual goal of commercialization.

193 Development of Inhibitory Reagents for the Study of Protein Function

(Fast-Track proposals will be accepted)

The central dogma of biology mandates that in cellular systems the ultimate perpetrators of action are proteins. This is true in both normal and transformed cells. While genomic efforts have shed new light on genetic mechanisms and risk factors, aside from the actual identification of genes, they say very little about the ultimate function of the protein products. Even predictions made from genetic sequences can only tell part of the answer. One of the most powerful ways currently to infer a gene's function has been to alter its expression, commonly through the painstaking construction of genetically modified model organism. Transgenic and "knock-out" animals have proved invaluable in the understanding of gene function. Despite the success of these approaches, they remain hampered by the constraints outlined above. This is compounded by such cellular events as transcription/translation control, alternate splicing, and protein turnover, which further remove the effector protein from its genetic origin. Recently, increased efforts have been underway to develop sophisticated approaches for specific control at the level of the transcript or the actual protein. Many of these approaches use interfering RNA or specific protein inhibitors. When fully realized, these approaches allow a much more specific and quantitative control over a protein's function. These approaches should prove a valuable complement to genetic approaches helping to understand biological behavior of specific proteins. This type of knowledge is critical for the greater understanding of the transformation process. Many of the potential designs could also have application in subsequent therapy. This solicitation topic would encourage the development and commercialization of new technology for the development of small molecules and RNA inhibitors to modulate protein function.

In the Phase I, the offeror should propose feasibility studies to develop or improve a technology capable of specifically modulating the expression or functionality of a protein. The approach should be compatible with various cellular and/or model systems. Delivery systems, while not an essential component of the system, should also be considered. The phase II would call for further development with ultimate commercialization and availability to the cancer research community.

194 Development and Application of High-Throughput Proteomics Technologies

(Fast-Track proposals will be accepted)

Identification and characterization of the distinguishing molecular signatures of human cancer is a major focus within NCI's clinical and basic research programs. This effort cuts across all disease sites and tissue types, and has essential applications to diagnosis, prevention and treatment, as well as to cell biology and biochemistry. Given that a wide array of affinity-based, high-throughput approaches to the systematic analysis of human gene expression are currently under development within the private sector and that many key biological questions and diseases are under study in the NCI, NCI seeks to support research and development efforts in small, private concerns as a means to accelerate proof-of-principle of emerging proteomic technologies and to support further development of those demonstrated to be of value in cancer research.

The NCI seeks to fund the development of a wide array of nascent proteomic technologies that offer improved performance and efficiency over those currently available.

Phase I awards will be made to demonstrate technical merit, determine potential applications, and overall feasibility of methods and/or approaches. A report addressing technical feasibility will be required at the end of the award period.

Phase II awards will be made to demonstrate applicability to problems in cancer research and to support continued development of tools, methodologies, and system components. Deliverables will be specific to each proposal and could include but not necessarily be limited to instrumentation, software applications, or reagents. A report addressing applicability of the

specific method or approach will be required at the end of the award period.

Proteomic technologies to be solicited would include, but not necessarily be limited to, high-affinity reagents, as well as equipment and methods supporting high-throughput screening, detection or reagent preparation designed for the systematic analysis of levels of expression of large numbers of proteins in a variety of normal and diseased cell types and tissues. Biological systems for analysis will be based on either human cancer or mouse models thereof. Some areas likely to be covered in proposals include:

- Protein arrays and other tools and technologies for the rapid, sensitive, and high-throughput detection of proteins in vitro and in vivo;
- Technologies for mapping protein distribution and protein-protein interactions in vivo;
- Instrumentation for parallel synthesis and processing of proteins;
- Techniques for sample preparation or sub-fractionation of complex protein extracts. Approaches should be compatible with procedures such as mass spectrometry, two-dimensional gel electrophoresis, etc.;
- Technologies for the detection and analysis of protein-nucleic acid interactions and protein-protein interactions (e.g., receptor-ligand interactions, antibody-antigen interactions, and enzyme-substrate interactions);
- New protein labeling reagents and modalities for increased sensitivity and specificity;
- Technologies for the “real-time” monitoring of protein trafficking within the cell;
- Serum fractionation schemes and analytical tools;
- Bioinformatics and data mining tools for management and interpretation of large sets of proteomic data.

NATIONAL INSTITUTE ON DRUG ABUSE (NIDA)

NIDA's mission is to lead the nation in bringing the power of science to bear on drug abuse and addiction, through support and conduct of research across a broad range of disciplines and by ensuring rapid and effective dissemination and use of research results to improve prevention, treatment, and policy.

This Solicitation invites proposals in the following areas:

034 Develop New Technologies for Drug Abuse Prevention Delivery

(Fast-Track proposals will be accepted)

The past several years have witnessed considerable interest in using technology in educational settings with children, youth, and adults. New technologies, including CD-ROM, the Internet, videotape, videodisc, and other electronic means have great potential for delivering and disseminating drug abuse prevention programs. However, the application and development of such technologies has lagged behind their use in other settings and contexts. These new technologies potentially provide a more cost effective way of delivering prevention services.

Previous PRB SBIR contracts have focused on prevention research dissemination (mechanisms which are utilized to transfer drug abuse prevention information to practitioners, policy makers, and the public) and measurement modules for prevention interventions (aiding various groups to identify existing or develop new measures of the antecedents, mediators and outcomes thought to be associated with the interventions). This solicitation seeks to take programs with proven efficacy and translate research to practice through the use of new technologies.

Phase I would explore the practicality of technological solutions to the delivery of drug abuse prevention programs. Selected technical approaches would be developed and pilot tested. One could take a proven prevention program and place it into a new technology. Phase II would witness further development and the testing of these technologies in applied clinical (i.e. prevention) settings including further

developing those technologies that were successfully pilot tested in Phase I.

041 Design, Synthesis, Preclinical, Testing and Scale-Up of Novel Treatment Agents for Stimulant Abuse

(Fast-Track proposals will be accepted)

The purpose of this contract is to design, synthesize, evaluate and scale-up of compounds that may prove to be effective treatments for stimulant (cocaine and methamphetamine) abuse. Corticotropin-releasing factor (CRF) and numerous neurotransmitter systems, including the opioid, dopamine, GABA, and glutamate systems, appear to be involved with drug abuse/addiction. Compounds of interest include, but are not limited to, GABAergic, CRF-1 antagonists, mGluR5 antagonists and kappa-opioid antagonists. Phase I would be used to design, synthesize and conduct initial pharmacological screening of new entities as possible treatment agents for stimulant abuse. Phase II would involve scale-up, pharmacological and toxicological evaluations, and pharmacokinetic/toxicokinetic studies necessary for the advancement of these compounds into clinical candidates.

042 Antibody-Based Therapies for Substance Abuse Treatment

NIDA is seeking SBIR contract proposals on antibody-based therapies for the treatment of substance abuse, such as treatments for abuse of stimulants (cocaine, methamphetamine, club drugs), hallucinogens, opiates or tobacco. The antibody treatment could be either monoclonal antibodies for passive immunization or vaccines for active immunization.

In Phase I, the Contractor is expected to establish the production method for GMP production for a monoclonal antibody or a vaccine, and outline the toxicity testing needed for an IND submission. In Phase II, the Contractor is expected to provide GMP scale-up of sufficient material for toxicity testing and clinical safety testing, and carry out mandatory toxicity testing and human laboratory studies to examine the safety and efficacy of the antibody-based therapy. At the end of Phase II, the Contractor may independently develop the new treatment therapy, or may request to enter into a cooperative agreement with NIDA for the further

development of a new antibody-based therapy with commercial promise as a treatment agent.

043 Virtual Reality for the Treatment of Co-Morbid Drug Abuse and Post-Traumatic Stress

(Fast-Track proposals will be accepted)

Exposure, either in vivo or imaginal, is a standard treatment for PTSD. However, due to the cost and difficulty in recreating past events, in vivo exposure is not always a practical approach for treating Post-Traumatic Stress Disorder resulting from certain trauma experiences such as combat. Imaginal exposure is limited by a person's ability and willingness to imagine and attend to highly stressful memories. Recent findings (Rothbaum, B.O. 2001, Journal of Clinical Psychiatry) have suggested that Virtual Reality (VR) can be a useful clinical tool for treating Post-traumatic Stress. In this particular study, VR exposure was used to simulate exposure to war-like conditions in Vietnam Veterans with Post-Traumatic Stress Disorder (PTSD). People with drug abuse and/or dependence have high rates of co-morbid PTSD that in some cases may interfere with their participation in treatment and/or may be a trigger for relapse. NIDA seeks the development and application of VR technologies to address post-traumatic stress symptoms in people who abuse or are dependent on drugs. Phase I testing should establish the feasibility of the use of this technology for treating PTSD in people with co-morbid PTSD and Drug Abuse or Dependence and should also produce data that demonstrates that this methodology is effective for the PTSD (e.g., it reduces persistent re-experiencing of trauma, avoidance of trauma associated stimuli, and symptoms of arousal) and does not worsen drug abuse. Phase II should involve larger-scale testing (e.g. more research participants and treatment trials) examining various treatment parameters (e.g. timing of VR treatment within the drug abuse treatment experience and types of VR environments). The focus of Phase II testing should be the refinement of this treatment for use in the treatment of drug abusers.

044 Pharmacovigilance Database for Anti-Addiction Medications

(Fast-Track proposals will be accepted)

Successful development of new anti-addiction medications follows traditional drug development life-cycle epochs ranging from preclinical discovery to large multi-center clinical trials. A principal objective of early first-in-man studies is the characterization of safety typically in a very small number of subjects. While safety remains an endpoint of concern throughout development, NIDA clinical studies rarely evaluate more than 3,000 patient volunteers in a clinical development program spanning up to ten years. As clinical investigations of new treatment agents proceeds information from prior studies helps to focus safety assessments in subsequent studies to both minimize adverse reaction potential for study participants, and to expose severe reactions as early in the development cycle as practicable. As studies become larger the opportunity to test more diverse populations illustrates potential safety risks but even large Phase III studies conducted at multiple sites can fail to predict subtle effects. These effects may result from individual differences among patients, differences in study population due to dose or duration of exposure, or interactions from concomitant substances not widely encountered in pre-approval clinical studies. Detecting small signals from these pre-approval studies is problematic simply due to the relatively small population of participants and the lack of prior information about specific risks. The benefits of better information about a treatment's safety are obvious. In addition, as other disease categories, risks are managed in light of treatment alternatives and careful monitoring of factors that affect risk and benefits is expected of sponsors. Information derived by examining the adverse reaction experience of the population at large can help formulate or alter future study designs and provide leads to discovery teams seeking to improve treatment alternatives.

NIDA seeks the development and application of pharmacovigilance tools to augment clinical trial safety data with public-domain post marketing data. During Phase I, the project is expected to identify data sources needed to provide source records to characterize safety of marketed drugs and vaccines, and to formulate a plan to transform data records into an analytic database suitable for generating hypotheses based on relationships between drugs and events. Phase II of the project will implement the plan developed in Phase I, including data cleaning and other preparation needed to support data mining by NIDA, and its researchers, on an

ongoing basis. The principal product of the effort will be the creation of an analytic database and the associated tools required to maintain a pharmacovigilance database to assess safety of marketed and to-be-developed anti-addiction treatment agents.

045 Measurement Modules for Psychiatric Comorbidity Evaluation

(Fast-Track proposals will be accepted)

Researchers and treatment agencies that provide substance abuse services are under increasing pressure to demonstrate the effectiveness of these programs. However, many of these groups lack the expertise to identify existing instruments that meet their needs or to develop new valid and reliable measures of co-occurring psychiatric problems that frequently accompany addiction. This current initiative is designed to encourage the development of long- and short-form measures of the common psychiatric comorbid conditions.

The primary purpose of the Phase I contract would be to develop user-friendly instruments which are feasible for use in community treatment programs.

Phase II would involve a series of controlled studies of the reliability and validity of the instruments developed in Phase I. The Contractor should develop, via paper and pencil methods as well as methods that use computers, telephones and the Internet, measures that produce useable databases. The Contractor should also provide the necessary software for analyzing these databases that provides meaningful analysis and output for the end user.

046 Worksite Based Health Promotion for Youth

(Fast-Track proposals will be accepted)

There are a number of substance abuse prevention programs that have been shown to be effective and yet there has been very little uptake or broad dissemination of such programs to youth nationally. Numerous evidence-based adolescent substance abuse prevention programs have been designed and many efficacious programs have been developed for adolescents in related domains such as HIV, sex and anger. Most of these programs are

delivered in the school setting. However, almost 25 million youth aged 16-24 years are employed in work sites, often low-paying jobs without a clear career trajectory (e.g. Burger King, McDonalds). About 15 million of these youth have dropped out of school and are in the process of making the transition into their early adult lives. Among this subgroup, alcohol abuse, smoking, anger, weight control, and risk for sexually transmitted diseases including HIV are high relative to their in-school peers.

This contract would target a cluster of adolescent risk behaviors: smoking, alcohol and drug abuse, sexually transmitted diseases, HIV, unintended pregnancies, weight related diseases, and problems with managing anger. Prevention programs have been developed to address these problem behaviors, and yet many youth experience more than one of these problems. This concept suggests worksites in service training as a delivery vehicle for delivering preventive interventions to high-risk youth. Use of this existing infrastructure should boost the dissemination of efficacious/effective prevention programs.

In order to increase the dissemination of effective youth prevention programs Phase I would identify successful prevention programs and adopt and translate a portion of them for use in youth worksites. Phase I would also include a brief pilot test. Phase II would complete the adaptation followed by a test and evaluation of the program(s).

047 Synthesis of New Chemical Probes

This proposed SBIR project is for the synthesis or development of new chemicals/drugs /drug metabolites, and/or new peptido-mimetics for studying the mechanism of action of drugs of abuse and drug addiction. Such chemical compounds are needed by the NIDA Drug Supply Program. This Program provides controlled drug substances, other chemical compounds, and analytical services without any cost to research investigators to promote research in drug abuse area.

Methods may include the following:

- 1 Synthesis of new chemical compounds/reagents as biological probes,
- 2 Synthesis of existing chemical compounds at reasonably lower cost compared to commercially available compounds and/or,

- 3 Screening of new chemical compounds utilizing combinatorial chemistry technique and/or other rapid screening methods to discover new ligands.

Proposals are invited for the synthesis of new chemicals and their screening as described above. Phase I should demonstrate the feasibility of the proposed innovation and Phase II, the development, characterization, testing, and screening of innovation. It should also be demonstrated that the new or modified chemical compounds are suitable for drug abuse research.

048 Virtual Reality for Treatment of Pain or Drug Addiction

Recent findings (Hoffman et al., 2000, Pain, 85, 305-309) have suggested that Virtual Reality (VR) can be a useful clinical tool. In this particular study, VR exposure was used to allow patients to selectively not attend to an otherwise painful procedure. Drug abuse, like pain, is a problem that is strongly impacted by stimuli in the abuser's environment and psychological factors. Thus, it is reasonable to assume that VR may be useful in allowing individuals to cope with and overcome drug craving, withdrawal symptoms or environmental cue-induced drug seeking that promotes drug abuse. Contract proposals are sought to examine the utility of VR technologies in the treatment of various types of drug abuse or for development of treatments for both acute and chronic pain. These treatments can be based in clinical settings or the patient's homes. Phase I testing should establish the feasibility of the use of this technology in the particular population to be tested. Phase I should also produce data that demonstrates that this methodology is effective for the particular type of pain being treated. Phase II should involve larger-scale testing (e.g. more subjects and treatment trials) examining various treatment parameters (e.g. timing of treatment, types of VR environments). The focus of Phase II testing should be the refinement of this treatment for use in pain patients.

For VR utility in drug abuse, the treatments can be developed to address drug withdrawal, drug craving or on-going drug related behaviors. The development of VR technologies should address abuse of all types of drugs (e.g. cocaine, marijuana, nicotine, alcohol, inhalants). Phase I testing should establish the feasibility of the use of this technology for the particular drug problem

addressed (e.g. cocaine craving, opioid withdrawal) and should also produce data that demonstrates that this methodology is effective for the particular drug problem. Phase II should involve larger-scale testing (e.g. more subjects and treatment trials) examining various treatment parameters (e.g. timing of treatment, types of VR environments). The focus of Phase II testing should be the refinement of this treatment for use in the treatment of drug abusers.

049 Technologies for Proteomic Analysis in the Nervous System

The discovery of protein function would be greatly accelerated by characterizing proteins based on functional characteristics. This announcement solicits applications for high-throughput methods for identifying protein-protein interaction, identifying low abundance proteins, identifying integral membrane proteins; and the development of protein recognition probes including but not limited to antibody libraries, aptamers, chemical libraries, and development of methods to quantitate proteins. Applications are also sought for identifying the functional activity of proteins using biosensor-base technology such as FRET. Phase I applications should demonstrate the feasibility of the proposed technology. Phase II should develop a final product that can be used by NIDA investigators.

050 Development of Science Education Materials Related to the Use of Animals in Research

(Fast-Track proposals will be accepted)

There is a lack of understanding among the general public and children regarding the critical role that animals play in biomedical research as well as the necessity for basic research to make progress toward improving health. This is particularly problematic in the drug abuse research area. Therefore, this contract solicitation seeks projects that will substantially improve understanding of the necessity for basic biomedical research and scientific literacy related to the use of animals in biomedical research among students and teachers at the 4th through 12th grade levels, parents, and/or the general public. Programs or projects must seek to accomplish these goals with a specific focus on drug abuse related research (e.g. neuroscience, medications development,

molecular biology, etc). Programs and projects aimed at school children should convey the topic in a way which makes learning science fun and interesting for the students and which captures their enthusiasm for science. Student programs and projects must also adhere to the National Science Education Standards. All programs and projects must include an evaluation component that can provide useful and accurate information on the efficacy of the program or project.

Phase I should include studies to determine the best format for the chosen audience (e.g. focus groups), studies that demonstrate feasibility, and the development of a prototype.

Phase II should include continued formative evaluations to guide the development of the program or project, development of the program or project, and a summative evaluation to determine the project/program's efficacy in improving science education/literacy.

051 Development of Testing Technology to Support Delivery of Linked Drug Abuse Treatment and Primary Medical Care

This contract seeks to develop field-expedient testing technology (including clinical laboratory tests and accompanying instrumentation) to support the delivery of linked drug abuse treatment and primary medical care to underserved individuals in various clinical settings (e.g. mobile medical vans; rural and urban community clinics; correctional facilities). Technology should be readily usable by staff and patients in drug abuse treatment programs; outreach workers; social service workers; and drug abusers in the community. The following are particular areas of interest:

1. Development of methods for detecting infectious diseases frequently encountered among drug users (e.g. HIV/AIDS; hepatitis B and C; tuberculosis; opportunistic infections; septicemia).
2. Development of methods for detecting and quantifying drugs of abuse and infectious agents in a variety of specimens, both biologic (e.g. blood, saliva, semen, mucus, urine, hair) and inert (e.g. paraphernalia; powders or liquids believed to contain drugs).
3. Development of methods for quantifying levels of treatment medications (e.g. antiretroviral agents; methadone).

4. Development of methods for performing laboratory-based nutritional assessments.
5. Development of methods for performing routine clinical chemistry and hematologic tests (e.g., liver enzyme studies, blood lipid profiles, urinalyses, complete blood counts, hemoglobin determinations).

Phase I would be used to demonstrate the feasibility of the proposed method and Phase II, the development and testing of the method.

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES (NIEHS)

Human health and human disease result from three interactive elements: environmental exposures, individual susceptibility and time. The mission of NIEHS is to reduce the burden of human illness and dysfunction from environmental exposures by understanding each of these elements and how they interrelate. NIEHS achieves its mission through multidisciplinary biomedical research programs, prevention and intervention efforts, and communication strategies that encompass training, education, technology transfer, and community outreach.

This solicitation invites proposals in the following areas: (Fast-Track proposals will be accepted)

084 Development of Software to Associate Haplotype Populations with Disease Pathways

Software is needed to develop comparative species analysis of single nucleotide polymorphisms (SNPs) that can be uniquely associated with alleles of genes that result in increased susceptibility toward disease and adverse or no-effect response for environmental toxicants, e.g. styrene, butadiene, acrylamide, or medicinals such as chemotherapy agents. Algorithms need to be developed that can locate SNPs via BLAST type searches of human and non-human databases and that can make associations with known disease genes and sub-populations of susceptible individuals via literature data mining search strategies. This in silico approach will locate SNPs in various systems and develop disease gene lists for human as well as surrogate model systems such as rat, mouse and yeast. It will also help locate special populations with regard to susceptibility to diseases and/or environmental exposures.

085 Development of Antibody Arrays for Toxicoproteomics

Toxicoproteomics is the global response of proteins to a toxicant from a cellular genome. A major technical challenge for toxicoproteomics is to be able to rapidly provide a level of information density comparable to gene expression arrays. The goal of this solicitation is the development, characterization and validation of either a complete protein array or sub arrays directed to determine the level of, for example, transcription factors, signaling pathway proteins, xenobiotic metabolism proteins, phosphorylated proteins etc. based on antibodies. Detection of low abundance proteins or protein modifications can theoretically be accomplished by antibody array chips as antibodies can be densely arrayed in a similar fashion to gene array chips. The development of antibody arrays for the detection of proteins or classes of proteins would have a major stimulatory effect on the field of toxicoproteomics as it would allow the detection of protein changes without expensive equipment or time-consuming analyses.

086 Use of Metabonomics to Develop Biomarkers of Organ Toxicity

Metabonomics combines the techniques of high resolution NMR with pattern recognition technology to rapidly evaluate the metabolic status of an animal (or human) such that the onset, duration, severity and target organ localization can be distinguished. In this context, there is an urgent need to develop and establish the role of metabonomics for predicting the potential of environmental agents to cause or enhance disease and dysfunctions. The NIEHS is interested in supporting the development, characterization and validation of new biomarkers of organ toxicity due to exposure to environmental agents. We are specifically looking for non-or minimally invasive metabonomic approaches using blood or urine to detect chemical perturbations indicative of organ toxicity. While all organs are of interest and will be acceptable under this initiative, the NIEHS is particularly interested in the use of metabonomics to develop biomarkers of CNS and liver toxicity. The metabonomic biomarkers should be anchored in physiology or pathology such that they would be indicative not only of site of toxicity but also suggest mode or mechanism of toxicity. Our long-term goal is that the study of metabolic changes in biofluids in response to pathophysiological insult will

highlight key pathways and place transcriptome and proteome data in perspective.

087 Automated Scoring of Chromosome Damage in Sperm Using FISH Biomarkers

New molecular methodologies have been and continue to be developed for fluorescence *in situ* hybridizations (FISH) with chromosome specific DNA probes for use in examining mammalian sperm cells. This new methodology improves the power of detection of chromosome damage in male germ cells but the speed with which the various evaluations are made would be greatly enhanced if the scoring would be automated. The components needed for automating this process, such as computer controlled microscope stages, laser image analysis, and brightly labeled chromosome specific DNA probes are available. The purpose of this solicitation is to develop the appropriate software and hardware to automate the detection of chromosomally abnormal sperm using FISH technologies. The product developed should clearly demonstrate the ability to capture, store, review and analyze information with high sensitivity, specificity and throughput.

088 Development of Microarray Profiles for Microbial Toxicity

The demonstration that exposure of animals to specific chemical classes can be characterized through microarray analysis of altered gene expression provides the basis for development of similar expression profiles of animals exposed to microbes (bacteria, viruses, and other agents). The development of such profiles could lead to the identification of new biomarkers of specific microbial exposure and ultimately possibly yield important diagnostic tools. This project requests proof-of-principal experiments to determine if microarray data from blood cells could be used to distinguish an individuals expose to specific classes of pathogenic agents. A good example would be to compare gene expression data for animals exposed to *B. anthracis* vs *B. subtilis*. If gene expression data could distinguish between individuals exposed to these closely related bacteria that would constitute proof-of- principle that this approach may be useful for the development of diagnostic tools that would have applications in the area of "bioterrorism" as well as the detection and intervention of disease.

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES (NIGMS)

The NIGMS supports research and research training in the basic medical sciences and related natural and behavioral sciences and in specific clinical areas (i.e., clinical pharmacology, trauma and burn injury, and anesthesiology). The NIGMS also supports health-related research that is otherwise not assigned to another of the PHS components.

For additional information about areas of interest to the NIGMS, please visit our home page at <http://www.nigms.nih.gov>. This site includes staff contact information by program area (http://www.nigms.nih.gov/nigms_staff/contact.html). It also includes links to program announcement that highlight NIGMS areas of special emphasis (<http://www.nigms.nih.gov/funding/funding.html>).

This solicitation invites proposals in the following area:

001 Polyclonal Antibodies from Non-Mammalian Model Systems

The purpose of this contract is to enable the successful offeror to acquire, characterize, catalog, and make available to researchers at reasonable cost polyclonal antibodies against specific antigens from non-mammalian eukaryotes that are used as model systems for biomedical research. Examples of such organisms include but are not limited to zebrafish, *Drosophila melanogaster*, *Caenorhabditis elegans*, *Neurospora*, and baker's yeast. Generation of new polyclonal antibodies against specific antigens from non-mammalian eukaryotic model systems, with the goal of developing the antibodies for commercial distribution, may also be initiated. The rationale for this phase I contract solicitation is that there is no commercial source for some of the most widely used polyclonal antibodies from non-mammalian eukaryotic model systems. Thus, laboratories in which popular antibodies are generated may receive hundreds of requests per year and spend a substantial amount of time responding to them. Conversely, investigators who want to use polyclonal antibodies must take the time to track down the source of each antibody they need and contend with inconsistencies in quality control, documentation, and the speed at which requests are filled. A centralized commercial source to

which investigators could donate polyclonal antibodies that they generate, at which users could purchase high-quality, well-described antibodies at reasonable cost, would benefit the ever-increasing number of investigators who generate and use antibodies in their research.

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE (NHLBI)

The National Heart, Lung, and Blood Institute plans, conducts, and supports research, clinical trials and demonstrations related to the causes, prevention, diagnosis, and treatment of heart, blood vessel, lung, and blood diseases and sleep disorders.

This solicitation invites proposals for the following topic areas:

028 Novel Allosteric B2-Adrenergic Receptor Agonists

(Fast-Track proposals will be accepted)

There is a need to discover novel small molecule drug-like compounds that allosterically increase the function of B2-adrenergic receptors.

Agonists of the B2-adrenergic receptor have become the mainstay of asthma therapy, and are the drug of choice for immediate, short-term bronchodilation. Stimulation of B2-adrenergic receptor sites on the sympathetic nervous system results in activation of the heterotrimeric protein Gs, which in turn activates adenylyl cyclase thus increasing the production of cyclic 3'5'-adenosine monophosphate (cAMP). This increase results in bronchial smooth muscle relaxation. Adverse effects occur through excessive activation of b-adrenergic receptors and are more common with the use of non-selective B-adrenergic agonists. The most common adverse effect observed with the use of selective agents is tremors. Vasodilation is observed when B2-receptors in the peripheral vasculature are stimulated. Tachycardia is observed most often as a result of stimulation of cardiac B1-receptors. Direct stimulation of cardiac B2-receptors and reflex mechanisms from the peripheral vasodilation also cause an increase in heart rate. Headache, nervousness, dizziness, palpitations, cough, nausea, vomiting, and throat irritation may also occur. All of these adverse effects are less likely with inhalation

therapy than with parenteral or oral therapy. Overuse of inhaled B2-agonists has been associated with increased mortality from asthma. One possible explanation of increased risk results from the cardiotoxic potential of B1-adrenergic agonists.

It would be of value to identify agonists for the B2-adrenergic receptor-Gs pathway that are specific for both this particular receptor subtype and the G protein. This contract program seeks small molecule drug-like compounds that will fill these requirements:

1. bind to B2-adrenergic receptor;
2. stimulate the activation of Gs by this receptor, while minimizing effects on the b1-adrenergic receptor and other Gs-coupled receptors in a whole-cell assay.

The deliverables for this contract program will be 3-5 compounds with the specified actions, 500 mg each.

A variety of proposal types are being solicited for this topic. Proposals for Phase I contract work as well as those submitted under the “**Fast Track**” initiative for the performance of both Phase I and Phase II work are requested. In addition, proposals for only a Phase II contract award are being solicited from offerors who can show satisfactory evidence of having done work to meet the Phase I work objective to establish the scientific or technical feasibility and commercial merit of the proposed research effort.

029 Novel PAR1 Antagonists

(Fast-Track proposals will be accepted)

There is a need to discover novel small molecule drug-like compounds that bind PAR1 specifically and block its interaction with Gq.

The serine protease thrombin is well recognized as being pivotal to the maintenance of hemostasis under both normal and pathological conditions. Its cellular actions are mediated through a unique family of protease-activated receptors (PARs). These receptors represent a novel family of G protein-coupled receptors that undergo proteolytic cleavage of their amino terminus and subsequent auto-activation by a tethered peptide ligand. The receptors are cleaved by thrombin at a specific site on the N-terminal extension, and a newly exposed N-

terminus acts as a tethered ligand to activate the receptor itself. PARs play important roles in “emergency situations” - such as trauma, when there is generation or release of proteases - as well as being involved in coagulation, inflammation, pain, healing and protection. The need for development of a PAR1 antagonist that may be valuable as a therapeutic agent has been recognized. Given the critical importance of PARs, it would be of value to identify and develop antagonists for PAR. However, the unique proteolytic activation of the receptor makes the ligand binding site a difficult target site as antagonists would need to compete with an intramolecular ligand while showing no intrinsic activity. Thus, alternate sites may be studied including the G protein pathway or downstream effectors.

This contract program seeks small molecule drug-like compounds that will fulfill these requirements:

1. bind to PAR1 receptor in its Gq combining region;
2. inhibits PAR1 signaling through Gq in cell culture;
3. with specificity for PAR1, that is, does not inhibit Gq signaling through at least three other Gq-coupled receptors in cell culture;
4. inhibits thrombin-mediated vascular permeability in animal models of ARDS.

The deliverables for this contract program will be 3-5 compounds with the specified actions, 500 mg each.

NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH)

The mission of the National Institute of Mental Health (NIMH) is to diminish the burden of mental illness through research. To achieve this goal, the NIMH funds basic research, clinical studies, and services delivery research concerning any aspect of behavioral and mental disorders (including HIV prevention and neuro AIDS research). Ultimately, this research will lead to greater understanding, better treatment and rehabilitation or prevention of mental disorders. The NIMH is also concerned with the speedy dissemination and use of this knowledge through scientific communications and public education, and in its more effective

implementation in practice and service delivery systems.

This solicitation invites proposals in the following areas: (Fast-Track proposals will be accepted)

027 Families as Research Partners: Development of Interactive Educational and Dissemination Modules to Train Family Members of Children with Emotional or Behavioral Disorders about Mental Health Research Methods, Procedures, Data Analyses, and Interpretation

The purpose of this contract is to develop evidence based interactive educational and dissemination modules to train families of children with emotional or behavioral disorders on research issues relating to studies on mental health service delivery, treatment development, preventive interventions, risk reduction, or epidemiology. The target population is broadly defined as families of children with specific psychiatric disorders, as well as behavioral or emotional problems secondary to developmental disorders, neuropsychiatric syndromes, or chronic medical illness. Because families are pivotal members of any treatment or intervention team, offering unique perspectives on their child's functioning and response to interventions, it is important that they be involved fully as partners in intervention development and delivery of care. Often this is not the case, particularly with minority and rural; families for whom there may be additional cultural, language and economic barriers.

Anticipated outcomes for Phase I include the development of draft: (1) interactive training materials; (2) evaluation/outcome criteria; and (3) protocols for the testing of these modules. Particular attention should be paid to developing appropriate materials and strategies to engage underserved minority and rural families in this process.

Among the modules needed are those that address issues such as: (1) random assignment and its ethical and scientific implications; (2) research design and development of new models of care; (3) ethical issues in validating treatment or preventive interventions; (4) research partnerships and the delineation of roles; (5) health care and studies of system variables; (6) identification, recognition and clinical issues in assessment and diagnosis.

The products created under this contract should recognize the diversity of families in terms of racial/ethnic minority status, socio-economic status, rural or other environmental factors, diversity of family types (e.g., grandparents, foster parents, family configuration) and special family situations that might impact training and research participation (e.g., mental health of other family members) and address specific ways these factors will be taken into consideration (e.g., focus groups with Hispanic families, grandparents, foster parents). Phase 1 should be limited in scope, with a specific target population defined. Families should be recruited in order to obtain a representative sample of the overall stakeholder population. Content area should also be defined and tailored to the target problems; as well as contextual variables of the families (e.g., ethnicity, education level, rural/urban residence); and types of intervention (e.g., prevention, treatment). Specifics about the training modules (e.g., number of sessions, specific modifications of existing products, evaluation criteria) should be included and should be based on empirically validated adult education processes. It is expected that an advisory group comprised of family stakeholders, individuals with expertise in adult education and funded researchers in relevant mental health areas will be included. Plans should be included for one or two trips to the NIMH for orientation and to present draft materials to program staff.

Reports that are relevant to this announcement include;

Blueprint for Change: Research on Child and Adolescent Mental Health: a report of the National Advisory Mental Health Council, May 2001

Surgeon General's National Action Agenda for Children, January 2001

Bridging Science and Service: a report of the National Advisory Mental Health Council

028 Developing Research Based Training Modules for Conducting Community Based Mental Health Interventions and Services Research with Underserved Racial/Ethnic and Rural/Frontier Populations

Background NIMH supported research on treatment, prevention and services for persons

with or at high risk for mental disorders is increasingly conducted in "real world" settings and has highlighted the issues of health disparities and gaps in meaningful community participation in the conduct of such research. (See- Social and Cultural Dimensions of Health Program Announcement: <http://grants.nih.gov/grants/guide/pa-files/PA-02-043.html>, Patient Centered Care Program Announcement: <http://grants.nih.gov/grants/guide/pa-files/PA-01-124.html>, Research on Mental Disorders in Rural and Frontier Populations: <http://grants.nih.gov/grants/guide/pa-files/PA-00-082.html>) Several recent reports (NIMH Strategic Plan for Reducing Health Disparities: <http://www.nimh.nih.gov/strategic/strategicdisparity.cfm>; Bridging Science and Service Report: <http://www.nimh.nih.gov/research/bridge.htm>) have emphasized the pressing need- in terms of equity, science, and public health- for studies to include samples of traditionally underserved racial/ethnic and rural/frontier populations. In fact, many salient questions regarding the efficacy, effectiveness and diffusion of mental health interventions and services can only be addressed within an appropriate community context.

University based researchers and their community partners often begin de novo in initiating, establishing, sustaining, evolving and evaluating their partnerships. Frequent barriers to that process include lack of effective two-way communication and lack of time and personnel dedicated to the collaborative process. The productivity and frequency of such research partnerships can be enhanced by **empirically based resources to aid in the scientific, practical and operational aspects of conducting mental health community based interventions and services research with underserved racial/ethnic and rural/frontier populations.**

Increasing participation in mental health research by underserved groups is necessary to achieve not only better mental health outcomes but to establish empirically validated services and interventions for various communities and enhance the dissemination and implementation these. Achieving broader participation will require wider community outreach, and mutual understanding and goal setting between researchers and underserved populations. This announcement is intended to contribute to the reduction of health disparities by enabling NIMH

to build a stronger portfolio of research relevant to the identified historically underserved populations.

Purpose Achieving the goal of community participation in research requires researchers, institutions, and racial/ethnic and rural/frontier communities to work together in new and different ways. Thus, there is a need for the development, dissemination, and implementation of empirically based educational/training modules to foster and guide these new types of working relationships. The target audience of these modules includes, but is not limited to, individual researchers conducting or developing plans for community-based mental health research, or institutions that can train researchers in conducting community-based research.

Phase I should include: (1) a summary review of the evidence on effective community engagement and development of a list of resource articles and case-studies; (2) developing an operationalized plan for the development of content for each of the community engagement modules (with input from researchers and targeted community populations), and designing for each module a format and presentation plan; (3) designing a plan to pilot and evaluate modules which includes the participation of NIMH supported researchers. The format for these modules is not limited and may be manual-based, web-based, or use a train the trainers model, or be a combination of strategies. Phase II of this Fast Track contract will include: (1) further refinement of content and development of modules and (2) actual pilot testing of modules with researchers or jointly with researchers and communities. In addition, plans should include 1 or 2 visits to the NIMH for orientation and presenting draft reports.

Curricular Needs A project may target one or several underserved populations. Examples of areas that the training modules could target include:

Background/Preparation

- goals and importance of community participation
- defining the specific target community: demographics, history, etc.

- understanding the historic relationship between research institution and community
- planning for the time and personnel needed
- establishing inclusion values within the project and staff (assessment of attitudes)

Beginning partnerships with communities

- identifying key stakeholders and key community informants (formal and “natural” leaders)
- deciding how and when to engage the community
- developing community advisory boards (authority, structure, function, duration)
- timing the steps of involvement

Getting community input

- understanding cultural appropriateness and acceptability for the specific community
- conducting community needs assessments
- developing mutual or compatible goals
- ethical issues (i.e.: how does the community define them?)
- data and safety monitoring: issues from the community

Sustaining the partnership

- maintaining an active community advisory board
- common problems/issues and how they might be addressed
- dealing with significant changes in the community or the research
- on-going communication between community and research

Determining success of the partnership/Enhancing future successes

- determining “success” as defined by various sectors of the community and by research standards
- assessing strengths and weaknesses to improve future collaboration
- building knowledge about community-research collaboration: sharing experiences

The products created under this contract should, where appropriate, include consideration of the particular requirements and methods of specific research domains, that is: prevention research, treatment studies, and services research. The products also should include consideration of issues related to working with a population and with specific sub-groups of such populations (i.e.: adults, children, adolescents, families, elderly, etc.) As input from both mental health researchers and traditionally underserved communities is viewed as an essential component of the development of the modules, the contractor must show capability for working with both groups.

029 Inventory of Successful Archived Mental Health Data Sets

The purpose of this Phase I SBIR contract is to: (1) develop an inventory of successful models of data archiving and preparation of data for public use and (2) evaluate these current “best practices” for use by mental health researchers.

NIMH has made significant investments in both large descriptive, longitudinal studies, as well as intervention trials. New NIH policies encouraging the public use of such data require that investigators consider ways of making data available and scientifically relevant for other investigators, as well as safe and ethical with regard to confidentiality of research participants, and fair to initial grant applicants.

This SBIR contract request involves the development of an inventory of successful models of data archiving and preparation for public use. The successful development of the inventory should be of use to NIMH staff in advising applicants, IRG reviewers, as well as investigators in the field. It may also serve other federal agencies and private entities if successful. Anticipated efforts include identification of issues related to hardware and software requirements, training and funding of

personnel to develop data and support materials, provision of technical assistance, ethical and safety/privacy issues, authorship, long term financing of an archive, and possible legal issues (inventions, FDA indications). Issues may vary for descriptive studies, versus intervention studies, and it is possible that separate inventories for each type of study may be needed. NIMH will develop an initial list of known successful archiving efforts, but will expect the contractor to seek out other archiving models from other federal agencies and private efforts. The contractor will be expected to meet with NIMH staff twice during Phase I to present draft reports.

030 Interactive Web-Based Networking Tool for Linking Collaborative/International Research Training Programs

The purpose of this SBIR contract is to develop a sustainable, web-based networking tool that will facilitate collaborative relationships among research training programs and permit the sharing of educational, operational, career development and research information in a safe interactive environment. During Phase I a prototype networking tool, content specification and implementation plan will be developed that is appropriate for mental and behavioral health interventions and services research training programs. The prototype should be based on and suitable for use by the collaborative International Clinical, Operational and Health Services Research Training Programs (ICOHRTA) supported by the NIH (NIMH, NIDA, NIA, Fogarty) but broad, generalizable and flexible enough to assure marketability in other research training venues. The ICOHRTA programs provide an excellent opportunity to develop and test a model among collaborative programs that have great diversity (e.g., systems, language, level of expertise, needs) yet are united by common goals. The composition of any proposed advisory committee should include ICOHRTA directors and other relevant staff and fellows. One or two meetings with NIMH/NIH staff may be proposed for orientation and presentation of draft prototypes.

Information about the ICOHRTA Program is available at:

<http://www.nih.gov/fic/programs/ICOHRTA.html> and

<http://www.nih.gov/fic/programs/grants.html#training>

and proceeding from the recent June 2002 workshop will be available by August 1, 2002.

031 Development of a Flexible Decision Support System for the Management of Psychiatric Diseases

The purpose of this SBIR is to develop a prototype for a flexible decision support system (DSS) for psychiatric disorders. The need for flexible decision support systems was highlighted at the recent, "15th Biennial International Conference on Mental Health Services Research Meeting" in April, 2002. Discussion at the meeting focused on, *"the development of systems to support evidence based medicine approaches that provide real time information on therapeutic decisions from both global and local sources to practicing clinicians during patient encounters"* (e.g., the need to develop data systems that incorporate local knowledge and global knowledge on best ways to care for individuals with psychiatric disorders -- systems that can incorporate new information as it becomes available).

Proposed integrated DSS systems should include, but not necessarily be limited to, the following components: (1) a clinically efficient treatment management system that helps the clinician gather and assemble relevant data (e.g., inclusion of symptom checklists and other clinical outcome measures that can easily and automatically be transferred to a clinical data base and "tickler" files to track clinical data such as patients not returning for visits or filling prescriptions in a timely manner); (2) a system that allows the tracking of data at the level of patient, clinician, site, and organization; (3) a data management and analysis "engine," that harvests data from existing guidelines and the organization's previous clinical experience, and (4) a clinical DSS interface that delivers the available treatment options and evidence to the clinician at the point of care in real time and in a user-friendly manner. A specific mental disorder or group of disorders may be the focus of the prototype, however the system must be flexible enough to adapt to a broad range of psychiatric disorders. Advisory committees should include relevant researchers in the areas of mental health interventions and services as well as potential consumers of the systems. One or two trips to meet with NIMH staff may be proposed

for the purpose of orientation and presentation of draft materials as long as the need to do so is documented.

CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)

NATIONAL CENTER FOR CHRONIC DISEASE PREVENTION AND HEALTH PROMOTION, CENTERS FOR DISEASE CONTROL AND PREVENTION (NCCDPHP)

The NCCDPHP plans, directs, and coordinates programs in health promotion, chronic disease prevention, and reproductive health to enhance quality of life, improve reproductive health, and reduce the incidence of heart disease, stroke, cancer, diabetes, arthritis, obesity, oral disease, infant and maternal morbidity and mortality, unintended pregnancy, and emerging chronic diseases. NCCDPHP uses two essential criteria to prioritize its research portfolio, societal burden and disproportionate burden. NCCDPHP places high priority on chronic diseases and conditions and reproductive health outcomes that have the greatest total impact on health, longevity, and quality of life. NCCDPHP places high priority on eliminating disproportionate burden related to sex, age, race, ethnicity, geography, sexual orientation, socioeconomic status, disability, and special needs. NCCDPHP supports three primary types of applied research, research on cause (determinant research), research on effect (intervention research), and research on application and benefit (dissemination research). NCCDPHP emphasizes cross-cutting research that is participatory, accounts for social and ecological factors, and is implemented at multiple levels.

NCCDPHP has identified ten priority research areas: (1). Develop new measures and research designs to strengthen the quality of research; (2). Identify the underlying determinants of racial and ethnic health disparities; (3). Develop and evaluate interventions to eliminate health disparities; (4). Examine established and emerging risk factors for chronic disease and investigate their potential for public health interventions; (5). Assess the effectiveness of policy and environmental interventions to promote health; (6). Improve the processes and outcomes of health care systems; (7). Develop effective communication strategies to promote health; (8). Examine methods for helping people

manage their own health; 9). Develop and evaluate the effectiveness of population-based health promotion and disease prevention policies and programs at local, state, national, and international levels; 10). Examine approaches for effectively translating successful community interventions into widespread practice. For examples of specific research questions in each of the ten priority areas, see Setting the Agenda: CDC Research in Chronic Disease Prevention and Health Promotion, available at <http://www.cdc.gov/nccdphp/index.htm>.

This solicitation invites proposals in the following areas:

OFFICE ON SMOKING AND HEALTH

013 High Through-Put Method to Isolate Tobacco and Tobacco-Derived Cigarette Components

Proposals are invited for the development of a method (i.e., method, technique, instrument, or device) to separate cigarette filler consisting of tobacco and tobacco-derived components (i.e., bright, burley, and Oriental tobacco, stems, puffed tobacco, paper reconstituted tobacco, and bandcast reconstituted tobacco). The method should also be applicable to other combustible tobacco products such as bidis, clove cigarettes, and cigars. The method should be of sufficiently high through-put to allow practical quantities of tobacco and tobacco-derived components to be separated in less than 24 hours. An example of a practical quantity is the amount of tobacco and tobacco-derived materials contained in a pack (i.e., 20 cigarettes) of cigarettes. Each separated fraction should contain less than 5% carry-over of other materials.

The proposal should include (1) a plan to develop a method (i.e., method, technique, instrument, or device) to separate the various tobacco and tobacco-derived components of the combustible cigarette column (i.e., bright, burley, and Oriental tobacco, stems, puffed tobacco, paper reconstituted tobacco, and bandcast reconstituted tobacco); (2) documentation of the capacity and the accuracy of the method; (3) verification of the identity of the separated fractions and the degree of carry-over by light microscopy; and, (4) evidence that the method, device, or technique is applicable to all current varieties of American-style blended cigarettes

and potentially applicable to other combustible tobacco products such as bidis, clove cigarettes, and cigars. The invited proposals will not involve human subjects.

014 Method to Screen Tobacco Products for Reduced-Harm or Reduced-Exposure Claims

Proposals are invited for the development of the technology that will lead to a method (i.e., method, technique, instrument, or device) or methods to rapidly, yet accurately, monitor reduced-harm and reduced-exposure tobacco product claims. The method should address claims of lowered levels of specific chemicals in the smoke (e.g., nicotine or tobacco-specific nitrosamines) of tobacco products. The method should also employ technology to evaluate made or implied reduced-harm claims (e.g., respiratory tract toxicity and cancer). The method should be applicable to a wide variety of tobacco products including self-extinguishing cigarettes, and modified emission (i.e., “reduced-exposure”) products. The method must allow comparisons with traditional cigarettes or experimental reference cigarettes (e.g., Kentucky reference cigarettes). When fully developed, the method should be of sufficiently high through-put to allow a practical number of brands to be investigated and results to be generated in a reasonable length of time. At least 5 brands are considered a practical number of brands. A reasonable length of time is considered 3 to 6 months to conduct the tests. The invited proposals will not involve human subjects.

DIVISION OF NUTRITION AND PHYSICAL ACTIVITY

015 Testing Youth Innovations to Increase Consumption of Vegetables and Fruits

Proposals are invited to design, develop, and evaluate (pilot test) a comprehensive educational strategy/program with school aged children and young adults (preschool to college) that focuses on increased vegetable and fruit consumption. This comprehensive educational strategy/program may be school or community based. It should be interdisciplinary, have a multi-dimensional approach, be theory based and generalizable to the national population. Partnering is encouraged with those entities interested in improving community health. Examples of existing interventions include the

Gimme 5, High 5 school-based interventions, and the Boy Scout 5-A-Day badge project. Innovations may include interventions in other youth organizations or programs.

016 Environmental Partnering Innovations to Improve Consumption of Vegetables and Fruits

Proposals are invited to design, implement, and evaluate an environmental change intervention incorporating 5-A-Day. Environmental change interventions can be an effective way to support a community effort to increase community vegetable and fruit intake. This intervention should be an educational and ecological effort emphasizing such factors as access to vegetables and fruits, cost/pricing of vegetables and fruits, and point-of-purchase education. Behavior-specific ecological models should be used to guide this intervention. This intervention may use innovative methodology and partnering to facilitate consumption of vegetables and fruits and encourage physical activity near large public land-use areas (examples include: strategies for edible trails, landscapes and community gardens).

NATIONAL CENTER FOR INFECTIOUS DISEASES (NCID)

031 Biodefense: Rapid Detection of Plague Organisms in Throat Swabs

The current first-line test for identifying *Yersinia pestis* in specimens taken from suspect patients/animals is a direct immunofluorescence assay (DFA) based on detection of the F1 antigen. The DFA is a well-validated test that has been in use since 1968 by the Diagnostic and Reference Laboratory, Division of Vector-Borne Infectious Diseases, NCID, CDC to establish a presumptive diagnosis of *Y. pestis* in tissues and cultures. Though DFA is a relatively rapid (less than 1 hour) test with high specificity, its interpretation requires expertise in microscopy and has a subjective element that may make it unreliable if readers, recruited during an emergency to examine throat swabs, have not had substantial experience with the technique. Furthermore, the performance of the DFA on throat swabs, a non-traditional specimen, has not been thoroughly evaluated. An immunoassay developed under this solicitation would not be a substitute for confirmatory tests such as culture and PCR, but

would help target appropriate use of these diagnostic methods.

Proposals are solicited to develop an optical immunoassay for plague modeled after an FDA-approved test for throat swabs for Group A Strep. This assay would be used to make a presumptive diagnosis of exposure to aerosolized plague organisms. In phase I, a prototype assay should be developed and its sensitivity for detecting *Yersinia pestis* should be demonstrated with simulated throat swabs saturated with diluted broth cultures of avirulent plague organisms. Preliminary estimates of specificity also should be developed using _spiked_ samples. A successful prototype may be eligible for Phase II funding to more extensively study the performance characteristics of the immunoassay.

032 Novel Antigen Delivery for Improved Influenza Vaccination in Aged Populations

The number of people in the United States aged >65 years was 30 million in the year 2000, and these numbers are projected to increase to 80 million, or 25% of the population, by the year 2050. Individuals aged >65 years are at increased risk of severe complications and death from influenza. Annual vaccination with the trivalent inactivated influenza vaccine is recommended for this high-risk group. Although the vaccine is 50-80% effective in preventing influenza-related hospitalizations and death in the elderly, the vaccine is only 30-40% effective in preventing influenza-like illness in frail elderly. In contrast, the vaccine is about 70-90% effective in preventing illness in healthy younger adults. The reduced efficacy of influenza vaccines in the elderly is likely due to reduced immune responses to vaccination in this age group. Studies in elderly have shown reduced cellular and humoral immunity following exposure to traditional intramuscular delivery of aqueous influenza antigens compared to younger adults. Therefore the development of novel delivery systems to improve the immune response to influenza vaccines in the elderly are highly desirable.

Delivery of antigens by novel routes such as intra- or trans- dermal or mucosal routes may optimize presentation of antigen to the immune system and improve vaccine immunogenicity. Alternatively, antigen-delivery vehicles that provide an adjuvant effect, whether delivered by

alternative or traditional routes, also have the potential to improve the immunogenicity and efficacy of influenza vaccines. Research will focus on applying one or more of the above approaches to the delivery of either traditional protein-based (inactivated or subunit) vaccine and/or DNA vaccines in order to achieve improved influenza vaccine immunogenicity and protective efficacy in a mouse model. The aged mouse is recognized to be a relevant preclinical model in which to evaluate vaccine strategies that may overcome the normal limitations of immunosenescence. Comparison of vaccine responses in young and aged mice is encouraged. Vaccine strategies that provide enhanced humoral immune responses and also cellular responses that have the potential to confer broader subtype cross-immunity would be important in an influenza pandemic situation.

NATIONAL CENTER FOR HIV, STD AND TB PREVENTION (NCHSTP)

The Division of STD Prevention provides national leadership through research, policy development, and support of effective series to prevent sexually transmitted diseases (including HIV infection) and their complications such as enhanced HIV transmission, infertility, adverse outcomes of pregnancy, and reproductive tract cancer. We assist health departments, health-care providers, and non-governmental organizations and collaborate with other governmental entities through the development, synthesis, translation, and dissemination of timely, science-based information; the development of national goals and science-based policy; and the development and support of science-based programs that meet the needs of communities.

This Solicitation invites proposals in the following areas:

013 Curriculum Development for Rapid Ethnographic Assessment

Existing training manuals and curricula for rapid ethnographic assessment often recommend consultation with an experienced ethnographer at some time during the process.

Phase I: Develop a curriculum that could be used by health educators at local health departments, clinics, community-based organizations, and other agencies or organizations that deliver STD prevention and

treatment services. The curriculum will target small-scale rapid assessment of STD prevention and treatment needs and provide sufficient content to eliminate the necessity of consultation with an expert in ethnographic methods. Content will include definition of problem and target population, data collection and analysis methods, and presentation strategies. The curriculum will define goals and measurable objectives, and describe subject matter, process, and overall evaluation plans. Elements or activities will be linked to the methodological framework.

Phase II: Evaluate the curriculum by conducting a pilot to demonstrate how goals and measurable objectives will be achieved. Key outcome variables will include educator and participant variables such as completeness of content coverage in allotted time, effectiveness of teaching, performance of tasks following participation in curriculum.

014 STD Counseling Guide for Pharmacists

Community-based pharmacists have a unique opportunity to counsel patients on treatment issues, as they are often the first and final professional contact for patients in the health care delivery system. This opportunity can be critical to the appropriate treatment of STDs. Patients often seek advice from pharmacists on symptoms related to STDs prior to visiting physicians. Patients also receive counseling from pharmacists on the appropriate use of medications for STDs. Although pharmacists have a valuable role in STD prevention and treatment, pharmacy school curricula often do not provide formal training on STDs.

Phase I: Develop a video and accompanying pocket-guide for pharmacists on counseling patients about treatment for sexually transmitted diseases. The video will provide information on the pathogenesis, prevalence and incidence, transmission, risk factors, treatment and counseling, follow-up and prevention for selected STDs. A main focus of the video will be on training pharmacists to counsel patients about the appropriate use of medications for STD treatment. The training will include appropriate counseling techniques for STD patients; proper use of medications for STD treatment including dosing instructions (e.g., times of administration, length of treatment, follow-up for missed doses, etc) and important drug-drug (e.g., antibiotics and oral

contraceptives) and drug-food interactions; recognition of adverse drug events; and appropriate follow-up. The video will serve as a training tool and the pocket-guide will serve as a reference source. In Phase I the video and pocket-guide will be developed.

Phase II: Evaluate the video and accompanying pocket-guide using the following method:

- Pilot-test the video and pocket-guide,
- Edit the video and guide based on results from the pilot-test;
- Conduct a training using the video and pocket-guide with pharmacists at a national pharmacy meeting, e.g., American Pharmaceutical Association Annual Meeting;
- Use pre and post test methods to determine change in pharmacist's knowledge and skills after receiving training; and
- Administer post-test to control group of pharmacists who did not receive the training and compare the results with the post-test results of pharmacists who did receive the training.

Phase III: Field test the video in community-based pharmacies that provide specialized counseling services for ambulatory patients.

015 Video Training in Parent-to-Child Communication Skills

Parental monitoring and communication about sex are two key factors that have been shown to delay coital debut and decrease risky sexual behavior (e.g., Forehand et al., 1997; Dittus, Jaccard & Gordon, 1999). However, few tools exist to help parents increase their skills in this area.

Phase I: The purpose of the first phase of this project is to develop a video intervention program targeting parents of young adolescents (ages 10-13) that would teach parents how to better communicate with their children about sexual issues and encourage parental monitoring. Three versions of the program should be created; one targeting African-American families, and two targeting Latino families, with an English version and Spanish language version. Intervention messages should be developed by a combination of experts in parental issues, a team of parents of young

adolescents and a team of young adolescents (ages 10-13).

Phase II: Evaluate the effectiveness of the intervention program using an experimental or quasi-experimental design. Key outcome variables would include increased communication about sexuality, increased supervision of children, and delay of sexual initiation and/or decreased intentions to initiate sex among the children of parents in the intervention group.

NATIONAL IMMUNIZATION PROGRAM (NIP)

The National Immunization Program (NIP) of CDC, plans, coordinates, directs, and participates in efforts to prevent and reduce illness and premature death through immunization against disease. Activities include: (1) conducting epidemiology, national surveillance, research and technical consultation on designated diseases for which effective immunizing agents are available, and on the safety of vaccines; (2) assessing immunization levels at national, state, and local levels; (3) guiding the development of recommendations, guidelines, technologies, and policies for effective, safe, efficient, and economical use of existing vaccines, and for the development and incorporation of new and improved vaccines and associated technologies into disease control programs; (4) providing technical, epidemiologic, scientific, statistical, financial, programmatic, and administrative assistance to state and local health departments in support of their immunization programs to prevent diseases recommended for vaccination; (5) implementing national outreach, mobilization, and public information activities to increase understanding about the benefits and risks of vaccines, to promote the demand for them, and to improve immunization practices among health care providers; (6) designing, developing, and implementing information systems to ensure that persons are properly immunized with the recommended vaccines for them; (7) collaborating with the World Health Organization (WHO) and its regional offices and with other CDC Centers/Institutes/Offices (CIOs) in worldwide eradication efforts for polio, and in planning for eradication of other diseases.

This solicitation invites proposals for the following topic areas:

016 Develop Methods for Administration of Vaccines, Including Live Virus Vaccines, Through the Respiratory Tract

Vaccination is one of the most cost-effective public health measures available, and global eradication of some diseases is technically feasible using current vaccines. Needle and syringe methods of vaccination have several drawbacks, however, including need for skilled personnel, risk of blood-borne disease, high cost, patient aversion to injection, and the need to safely dispose of large quantities of used needles and syringes. One of the National Immunization Program Research priorities is the development of alternative methods of vaccination. There is a need to develop methods for administration of vaccines, including live virus vaccines, through the respiratory tract. These methods include, but are not limited to, aerosols, dry powders, nasal sprays.

017 High-Speed, Disposable-Cartridge, Needle-Free Jet Injectors

Develop high-speed, needle-free, liquid jet injectors using disposable vaccine cartridges of unquestioned safety to avoid patient cross-contamination. Capabilities should include (1) options for intramuscular, subcutaneous, and intradermal administration with conventional liquid and reconstituted lyophilized vaccines, (2) speeds of at least 600 injections per hour, (3) hands-free loading and unloading of cartridges, (4) affordable pricing suitable for developing country mass vaccination, and (5) end-user filling systems for interim use until vaccine manufacturer prefilling becomes available. Priority will be given to proposals involving enlightened non-exclusive cross-licensing and royalty arrangements for existing commercial or investigational cartridge designs. This is to contribute towards a universal standard for vaccine cartridges to encourage manufacturer prefilling of same as the primary vaccine packaging.